

st is in DialUnits

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16jul08 14:34:13 User208760 Session D2959.1
    $0.53      0.148 DialUnits File1
$0.53 Estimated cost File1
$0.53 Estimated cost this search
$0.53 Estimated total session cost    0.148 DialUnits
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File 410:Dialog Comm.-of-Interest Newsletters 2008 /Mar  
(c) 2008 Dialog

Set	Items	Description
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? set hi ;set hi

HIGHLIGHT set on as ''

HIGHLIGHT set on as ''

? begin 5,73,155,399

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16jul08 14:34:23 User208760 Session D2959.2
    $0.00      0.117 DialUnits File410
$0.00 Estimated cost File410
$0.03 TELNET
$0.03 Estimated cost this search
$0.56 Estimated total session cost    0.265 DialUnits
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SYSTEM:OS - DIALOG OneSearch

File 5:Biosis Previews(R) 1926-2008/Jul W2

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File 73:EMBASE 1974-2008/Jul 14

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File 155:MEDLINE(R) 1950-2008/Jul 14

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IPCR/8 classification codes now searchable as IC=. See HELP NEWSIPCR.

Set	Items	Description
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? s (htr?)(10n)(antibod? or hybridoma? or immunoglobulin?)(20n)(75? or  
p75?)(20n)(tnf?)

10683	HTR?
2336912	ANTIBOD?
55195	HYBRIDOMA?
883389	IMMUNOGLOBULIN?
881454	75?
15171	P75?
272208	TNF?

S1	87	(HTR?)(10N)(ANTIBOD? OR HYBRIDOMA? OR IMMUNOGLOBULIN?)(20N)(75? OR P75?)(20N)(TNF?)
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? rd s1

S2	32	RD S1 (unique items)
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? t s2/3/all

2/3/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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15416609 BIOSIS NO.: 200000134922

The p55 tumor necrosis factor receptor (CD120a) induces endothelin-1  
synthesis in endothelial and epithelial cells

AUTHOR: Lees Delphine M; Pallikaros Zakos; Corder Roger (Reprint)

AUTHOR ADDRESS: Queen Mary and Westfield College, William Harvey Research  
Institute, St. Bartholomew's and Royal London School of Medicine and  
Dentistry, Charterhouse Square, London, EC1M 6BQ, UK\*\*UK  
JOURNAL: European Journal of Pharmacology 390 (1-2): p89-94 Feb. 25, 2000  
2000  
MEDIUM: print  
ISSN: 0014-2999  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/2 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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14434776 BIOSIS NO.: 199800229023  
Activators of polymorphonuclear neutrophils modulate expression of the  
tumor necrosis factor-alpha p75 receptor  
AUTHOR: Zeman Krzysztof (Reprint); Paleolog Ewa Maria; Tchorzewski Henryk  
AUTHOR ADDRESS: Dep. Clinical Immunology, Military Med. Acad., Pl. Hallera  
1, 90-647 Lodz 39, Poland\*\*Poland  
JOURNAL: Central-European Journal of Immunology 22 (4): p272-277 1997 1997  
MEDIUM: print  
ISSN: 1426-3912  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/3 (Item 3 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2008 The Thomson Corporation. All rts. reserv.

13838712 BIOSIS NO.: 199799472772  
IL-4 and TNF-alpha-mediated proliferation of the human megakaryocytic line  
M-07e is regulated by induced autocrine production of GM-CSF  
AUTHOR: Wadhwa Meenu (Reprint); Dilger Paula; Meager Anthony; Walker Barry;  
Gaines-Das Rose; Thorpe Robin  
AUTHOR ADDRESS: Div. Immunobiol. NIBSC, Blanche Lane, South Mimms, Potters  
Bar, EN6 3QG Herts, UK\*\*UK  
JOURNAL: Cytokine 8 (12): p900-909 1996 1996  
ISSN: 1043-4666  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/4 (Item 4 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13685482 BIOSIS NO.: 199799319542  
The role of receptors for tumour necrosis factor-alpha in the induction of  
human polymorphonuclear neutrophil chemiluminescence  
AUTHOR: Zeman Krzysztof (Reprint); Kantorski Jerzy; Paleolog Ewa M;  
Feldmann Marc; Tchorzewski Henryk  
AUTHOR ADDRESS: Dep. Clin. Immunol., Military Acad., Pl. Hallera I, 90-647  
Lodz 9, Poland\*\*Poland  
JOURNAL: Immunology Letters 53 (1): p45-50 1996 1996  
ISSN: 0165-2478

DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/5 (Item 5 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13598086 BIOSIS NO.: 199699232146  
Evidence for exclusive role of the p55 tumor necrosis factor (TNF) receptor  
in mediating the TNF-induced collagenase expression by human dermal  
fibroblasts  
AUTHOR: Rekdal Oystein (Reprint); Osterud Bjarne; Svendsen John Sigurd;  
Winberg Jan-Olof  
AUTHOR ADDRESS: Dep. Biotechnol., Inst. Med. Biol., Univ. Tromso, N-9037  
Tromso, Norway\*\*Norway  
JOURNAL: Journal of Investigative Dermatology 107 (4): p565-568 1996 1996  
ISSN: 0022-202X  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/6 (Item 6 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13509258 BIOSIS NO.: 199699143318  
Activation of the TNF-alpha-p55 receptor induces myocyte proliferation and  
modulates agonist-evoked calcium transients in cultured human tracheal  
smooth muscle cells  
AUTHOR: Amrani Yassine (Reprint); Panettieri Reynold A Jr; Frossard Nelly;  
Bronner Christian  
AUTHOR ADDRESS: Univ. Pa. Med. Cent., Pulmonary and Critical Care Div.,  
Dep. Med., East Gate Build., 3600 Spruce St., Philadelphia, PA  
19104-4283, USA\*\*USA  
JOURNAL: American Journal of Respiratory Cell and Molecular Biology 15 (1  
) : p55-63 1996 1996  
ISSN: 1044-1549  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/7 (Item 7 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13326226 BIOSIS NO.: 199698794059  
A non-competitive P55 TNF receptor antibody enhances the specific activity  
of lymphotoxin-alpha  
AUTHOR: Medvedev A E; Laegreid A; Sundan A; Espevik T (Reprint)  
AUTHOR ADDRESS: Inst. Cancer Res. Mol. Biol., Univ. Trondheim, N-7005  
Trondheim, Norway\*\*Norway  
JOURNAL: Scandinavian Journal of Immunology 43 (4): p439-448 1996 1996  
ISSN: 0300-9475  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/8 (Item 8 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13031498 BIOSIS NO.: 199598499331  
Activation of neutrophil and eosinophil respiratory burst by tumor necrosis factor-alpha on biological surfaces  
AUTHOR: Patriarca Pierlvigi (Reprint); Menegazzi R; Cramer R; Dri P; Busetto S; Decleva E  
AUTHOR ADDRESS: Ist. Patologia Generale, Univ. Trieste, Via A. Fleming 22, 34127 Trieste, Italy\*\*Italy  
JOURNAL: Regional Immunology 6 (5-6): p371-377 1994 (1995) 1994  
ISSN: 0896-0623  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/9 (Item 9 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2008 The Thomson Corporation. All rts. reserv.

12719254 BIOSIS NO.: 199598187087  
Modulation of monocyte antigen-presenting capacity by tumour necrosis factor-alpha (TNF): Opposing effects of exogenous TNF before and after an antigen pulse and role of TNF gene activation in monocytes  
AUTHOR: Kowalczyk Danuta; Mytar Bozena; Jasinski Marek; Pryjma Juliusz; Zembala Marek (Reprint)  
AUTHOR ADDRESS: Dep. Clin. Immunol., Inst. Peadiatr., Jagiellonian Univ. Med. Coll., Wielicka 265, 30-663 Cracow, Poland\*\*Poland  
JOURNAL: Immunology Letters 44 (1): p51-57 1995 1995  
ISSN: 0165-2478  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/10 (Item 10 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12565810 BIOSIS NO.: 199598033643  
Involvement of the tumor necrosis factor receptor p75 in mediating cytotoxicity and gene regulating activities  
AUTHOR: Medvedev Andrei E; Sundan Anders; Espevik Terje (Reprint)  
AUTHOR ADDRESS: Inst. Cancer Res., Univ. Med. Cent., Univ. Trondheim, N-7005 Trondheim, Norway\*\*Norway  
JOURNAL: European Journal of Immunology 24 (11): p2842-2849 1994 1994  
ISSN: 0014-2980  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/11 (Item 11 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12533039 BIOSIS NO.: 199598000872  
Functional activities of receptors for tumor necrosis factor-alpha on human

vascular endothelial cells  
AUTHOR: Paleolog Ewa M (Reprint); Delasalle Sally-Anne J; Buurman Wim A;  
Feldmann Marc  
AUTHOR ADDRESS: Kennedy Inst. Rheumatol., Sunley Div., 1 Lurgan Ave.,  
London W6 8LW, UK\*\*UK  
JOURNAL: Blood 84 (8): p2578-2590 1994 1994  
ISSN: 0006-4971  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/12 (Item 12 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12423301 BIOSIS NO.: 199497444586  
Lymphotoxin acts as an autocrine growth factor for Epstein-Barr  
virus-transformed B cells and differentiated Burkitt lymphoma cell lines  
AUTHOR: Gibbons Deena L; Rowe Martin; Cope Andrew P; Feldmann Marc; Brennan  
Fionula M (Reprint)  
AUTHOR ADDRESS: Kennedy Inst. of Rheumatol., Sunley Building, 1 Lurgan  
Ave., Hammersmith, London W6 8LW, UK\*\*UK  
JOURNAL: European Journal of Immunology 24 (8): p1879-1885 1994 1994  
ISSN: 0014-2980  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/13 (Item 13 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12377747 BIOSIS NO.: 199497399032  
Evidence that tumor necrosis factor alpha (TNF)-induced activation of  
neutrophil respiratory burst on biologic surfaces is mediated by the p55  
TNF receptor  
AUTHOR: Menegazzi Renzo; Cramer Rita; Patriarca Pierluigi; Scheurich Peter;  
Dri Pietro (Reprint)  
AUTHOR ADDRESS: Istituto di Patologia Generale, via A. Fleming 22, 34127  
Trieste, Italy\*\*Italy  
JOURNAL: Blood 84 (1): p287-293 1994 1994  
ISSN: 0006-4971  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/14 (Item 14 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12336554 BIOSIS NO.: 199497357839  
Role of the 75 kD- and 55 kD-receptors in tumour necrosis factor mediated  
cytotoxicity and its regulation by dexamethasone and by  
1,25-dihydroxyvitamin D-3 in U937 cells  
AUTHOR: Chambaut-Guerin Anne-Marie (Reprint); Guerrier Maguy; Thomopoulos  
Pierre  
AUTHOR ADDRESS: INSERM U282, Hopital Henri Mondor, 94010 Creteil, France\*\*  
France

JOURNAL: European Cytokine Network 4 (4): p285-292 1993 1993  
ISSN: 1148-5493  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/15 (Item 15 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12207596 BIOSIS NO.: 199497228881  
Ceramide does not mediate the effect of tumour necrosis factor alpha on  
superoxide generation in human neutrophils  
AUTHOR: Yanaga Fumi (Reprint); Watson Steve P  
AUTHOR ADDRESS: Dep. Pharmacol., Oxford Univ., Mansfield Rd., Oxford OX1  
3QT, UK\*\*UK  
JOURNAL: Biochemical Journal 298 (3): p733-738 1994 1994  
ISSN: 0264-6021  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/16 (Item 16 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12173160 BIOSIS NO.: 199497194445  
Regulation of monocyte chemoattractant protein-1 expression in adult human  
non-neoplastic astrocytes is sensitive to tumor necrosis factor (TNF) or  
antibody to the 55-kDa TNF receptor  
AUTHOR: Barna Barbara P (Reprint); Pettay James; Barnett Gene H; Zhou Ping;  
Iwasaki Koichi; Estes Melinda L  
AUTHOR ADDRESS: Dep. Clin. Pathol., L-12, Clevel. Clin. Found., 9500 Euclid  
Ave., Cleveland, OH 44195-5131, USA\*\*USA  
JOURNAL: Journal of Neuroimmunology 50 (1): p101-107 1994 1994  
ISSN: 0165-5728  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/17 (Item 17 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12152426 BIOSIS NO.: 199497173711  
Lymphotoxin lacks effects on 75-kDa receptors in cytotoxicity on U-937  
cells  
AUTHOR: Iwamoto Sanju (Reprint); Shibuya Isao; Takeda Ken; Takeda Minoru  
AUTHOR ADDRESS: First Dep. Biochem., Sch. Med., Showa Univ., Shinagawa-ku,  
Tokyo 142, Japan\*\*Japan  
JOURNAL: Biochemical and Biophysical Research Communications 199 (1): p  
70-77 1994 1994  
ISSN: 0006-291X  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/18 (Item 18 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11937204 BIOSIS NO.: 199396101620  
Roles of two tumor necrosis factor receptors in induction of  
differentiation of ML-1 cells  
AUTHOR: Takeda Ken (Reprint); Iwamoto Sanju; Takeda Minoru  
AUTHOR ADDRESS: 1st Dep. Biochem., Sch. Med. Showa Univ., 1-5-8 Hatanodai  
Shinagawa-ku, Tokyo 142, Japan\*\*Japan  
JOURNAL: Anticancer Research 13 (4): p883-886 1993  
ISSN: 0250-7005  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/19 (Item 19 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11842315 BIOSIS NO.: 199396006731  
Divergent responses of human astrocytoma and non-neoplastic astrocytes to  
tumor necrosis factor alpha involve the 55 KDa tumor necrosis factor  
receptor  
AUTHOR: Barna Barbara P (Reprint); Barnett Gene H; Jacobs Barbara S; Estes  
Melinda L  
AUTHOR ADDRESS: Dep. Immunopathology, Cleveland Clinic Foundation, 9500  
Euclid Avenue, Cleveland, OH 44195-5131, USA\*\*USA  
JOURNAL: Journal of Neuroimmunology 43 (1-2): p185-190 1993  
ISSN: 0165-5728  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/20 (Item 20 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11785043 BIOSIS NO.: 199395087309  
Expression and functional role of tumor necrosis factor receptors on  
leukemic cells from patients with type B chronic lymphoproliferative  
disorders  
AUTHOR: Trentini Livio; Zambello Renato; Agostini Carlo; Siviero Fosca;  
Adami Fausto; Marcolongo Renzo; Raimondi Roberto; Chisesi Teodoro;  
Pizzolo Giovanni; Semenzato Gianpietro (Reprint)  
AUTHOR ADDRESS: Ist. Med. Clinica, dell'Univ. Padova Clinica Med. 1, Via  
Giustiniani 2, 35128 Padova, Italy\*\*Italy  
JOURNAL: Blood 81 (3): p752-758 1993  
ISSN: 0006-4971  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/21 (Item 21 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11758447 BIOSIS NO.: 199395060713

Tumor necrosis factor alpha stimulates sphingomyelinase through the 55 kDa receptor in HL-60 cells  
AUTHOR: Yanaga Fumi (Reprint); Watson Steve P  
AUTHOR ADDRESS: Dep. Pharmacol., Univ. Oxford, Mansfield Road, Oxford, OX1 3QT, UK\*\*UK  
JOURNAL: FEBS (Federation of European Biochemical Societies) Letters 314 (3): p297-300 1992  
ISSN: 0014-5793  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/22 (Item 22 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11736801 BIOSIS NO.: 199395039067  
Autocrine growth limitation of human papillomavirus type 16-harboring keratinocytes by constitutively released tumor necrosis factor-alpha  
AUTHOR: Malejczyk Jacek (Reprint); Malejczyk Magdalena; Koeck Andreas; Urbanski Agatha; Majewski Slawomir; Hunzelmann Nicolas; Jablonska Stefania; Orth Gerard; Luger Thomas A  
AUTHOR ADDRESS: Dep. Histol. and Embryol., Inst. Biostructure, Warsaw Medical School, Chalubinskiego 5, PL-02004 Warsaw, Poland\*\*Poland  
JOURNAL: Journal of Immunology 149 (8): p2702-2708 1992  
ISSN: 0022-1767  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/23 (Item 23 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11721717 BIOSIS NO.: 199395023983  
Role of tumor necrosis factor-alpha and its specific 55-Kd and 75-Kd receptors in patients with lymphoproliferative disease of granular lymphocytes  
AUTHOR: Zambello Renato; Trentin Livio; Bulian Pietro; Cassatella Marco; Raimondi Roberto; Chisesi Teodoro; Agostini Carlo; Semenzato Gianpietro (Reprint)  
AUTHOR ADDRESS: Ist. Med. Clin. dell'Univ. Padova, Clin. Med. 1, Via Giustiniani 2, 35128 Padova, Italy\*\*Italy  
JOURNAL: Blood 80 (8): p2030-2037 1992  
ISSN: 0006-4971  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/24 (Item 24 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11703786 BIOSIS NO.: 199395006052  
Involvement of tumor necrosis factor (TNF) receptors p55 and p75 in TNF responses of acute myeloid leukemia blasts in vitro  
AUTHOR: Delwel Ruud (Reprint); Van Buitenen Carin; Lowenberg Bob; Touw Ivo  
AUTHOR ADDRESS: Dep. Hematol., Erasmus Univ., P.O. Box 1738, 3000 DR

Rotterdam, Netherlands\*\*Netherlands  
JOURNAL: Blood 80 (7): p1798-1803 1992  
ISSN: 0006-4971  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

2/3/25 (Item 25 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11431518 BIOSIS NO.: 199294133359  
THE TYPE B RECEPTOR FOR TUMOR NECROSIS FACTOR-ALPHA MEDIATES DNA  
FRAGMENTATION IN HL-60 AND U937 CELLS AND DIFFERENTIATION IN HL-60 CELLS  
AUTHOR: GREENBLATT M S (Reprint); ELIAS L  
AUTHOR ADDRESS: UNM CANCER CENTER, 900 CAMINO DE SALUD NE, ALBUQUERQUE, NM  
87131-5636, USA\*\*USA  
JOURNAL: Blood 80 (5): p1339-1346 1992  
ISSN: 0006-4971  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

2/3/26 (Item 26 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11372021 BIOSIS NO.: 199294073862  
ENHANCED EXPRESSION OF TUMOR NECROSIS FACTOR RECEPTOR MRNA AND PROTEIN IN  
MONONUCLEAR CELLS ISOLATED FROM RHEUMATOID ARTHRITIS SYNOVIAL JOINTS  
AUTHOR: BRENNAN F M (Reprint); GIBBONS D L; MITCHELL T; COPE A P; MAINI R N  
; FELDMANN M  
AUTHOR ADDRESS: CHARING CROSS SUNLEY RES CENTRE, LURGAN AVE, HAMMERSMITH,  
LONDON W6 8LW, GB, UK\*\*UK  
JOURNAL: European Journal of Immunology 22 (7): p1907-1912 1992  
ISSN: 0014-2980  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

2/3/27 (Item 27 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10759212 BIOSIS NO.: 199192004983  
INDEPENDENT REGULATION OF 55-KDA AND 75-KDA TUMOR NECROSIS FACTOR RECEPTORS  
DURING ACTIVATION OF HUMAN PERIPHERAL BLOOD B LYMPHOCYTES  
AUTHOR: ERIKSTEIN B K (Reprint); SMELAND E B; BLOMHOFF H K; FUNDERUD S;  
PRYDZ K; LESSLAUER W; ESPEVIK T  
AUTHOR ADDRESS: LAB IMMUNOL, INST CANCER RESEARCH, MONTEBELLO, N-0310 OSLO  
3, NORW\*\*NORWAY  
JOURNAL: European Journal of Immunology 21 (4): p1033-1038 1991  
ISSN: 0014-2980  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

2/3/28 (Item 28 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10644722 BIOSIS NO.: 199191027613  
PURIFICATION AND PARTIAL AMINO ACID SEQUENCE ANALYSIS OF TWO DISTINCT TUMOR  
NECROSIS FACTOR RECEPTORS FROM HL60 CELLS  
AUTHOR: LOETSCHER H (Reprint); SCHLAEGER E J; LAHM H-W; PAN Y-C E;  
LESSLAUER W; BROCKHAUS M  
AUTHOR ADDRESS: CENTRAL RES UNITS, F HOFFMANN-LA ROCHE LTD, ZFE/BIO 15/40,  
CH-4002 BASEL, SWITZERLAND\*\*SWITZERLAND  
JOURNAL: Journal of Biological Chemistry 265 (33): p20131-20138 1990  
ISSN: 0021-9258  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

2/3/29 (Item 29 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10622184 BIOSIS NO.: 199191005075  
BINDING AND REGULATION OF CELLULAR FUNCTIONS BY MONOCLONAL ANTIBODIES  
AGAINST HUMAN TUMOR NECROSIS FACTOR RECEPTORS  
AUTHOR: SHALABY M R (Reprint); SUNDAN A; LOETSCHER H; BROCKHAUS M;  
LESSLAUER W; ESPEVIK T  
AUTHOR ADDRESS: GENENTECH INC, 460 POINT SAN BRUNO BLVD, SOUTH SAN  
FRANCISCO, CALIF 94080, USA\*\*USA  
JOURNAL: Journal of Experimental Medicine 172 (5): p1517-1520 1990  
ISSN: 0022-1007  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

2/3/30 (Item 30 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10231409 BIOSIS NO.: 199090015888  
IDENTIFICATION OF TWO TYPES OF TUMOR NECROSIS FACTOR RECEPTORS ON HUMAN  
CELL LINES BY MONOCLONAL ANTIBODIES  
AUTHOR: BROCKHAUS M (Reprint); SCHOENFELD H-J; SCHLAEGER E-J; HUNZIKER W;  
LESSLAUER W; LOETSCHER H  
AUTHOR ADDRESS: CENTRAL RES UNITS, F HOFFMAN-LA ROCHE AG, 4002 BASEL,  
SWITZERLAND\*\*SWITZERLAND  
JOURNAL: Proceedings of the National Academy of Sciences of the United  
States of America 87 (8): p3127-3131 1990  
ISSN: 0027-8424  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

2/3/31 (Item 1 from file: 73)  
DIALOG(R)File 73:EMBASE  
(c) 2008 Elsevier B.V. All rts. reserv.

0076771155 EMBASE No: 1997064113  
IL-4 and TNF-alpha-mediated proliferation of the human megakaryocytic

line M-07e is regulated by induced autocrine production of GM-CSF  
Wadhwa M.; Dilger P.; Meager A.; Walker B.; Gaines-Das R.; Thorpe R.  
Division of Immunobiology, Blanche Lane, South Mimms, Potters Bar, EN6  
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Cytokine ( CYTOKINE ) (United Kingdom) December 1, 1996, 8/12 (900-909)  
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LANGUAGE: English SUMMARY LANGUAGE: English  
NUMBER OF REFERENCES: 52

2/3/32 (Item 2 from file: 73)  
DIALOG(R)File 73:EMBASE  
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0075520694 EMBASE No: 1993300250  
Role of the 75 kD- and 55 kD-receptors in tumour necrosis factor mediated  
cytotoxicity and its regulation by dexamethasone and by  
1,25-dihydroxyvitamin D SUB 3 in U937 cells  
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European Cytokine Network ( EUR. CYTOKINE NETW. ) (France) October 26,  
1993, 4/4 (285-292)  
CODEN: ECYNE ISSN: 1148-5493  
DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract  
LANGUAGE: English SUMMARY LANGUAGE: English  
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2/7/1 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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15416609 BIOSIS NO.: 200000134922  
The p55 tumor necrosis factor receptor (CD120a) induces endothelin-1  
synthesis in endothelial and epithelial cells  
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JOURNAL: European Journal of Pharmacology 390 (1-2): p89-94 Feb. 25, 2000  
2000  
MEDIUM: print  
ISSN: 0014-2999  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Synthesis of the vasoconstrictor peptide endothelin-1 by  
endothelial and epithelial cells is strongly induced by tumor necrosis  
factor alpha (TNF-alpha). The actions of TNF-alpha are mediated by two  
transmembrane receptors of approximately 55 (p55, CD120a) and 75 kDa  
(p75, CD120b). Reagents activating selectively these receptor subtypes  
have been used to identify which TNF receptor mediates the induction of

endothelin-1 synthesis. Stimulation of bovine aortic endothelial cells or human HEp-2 epithelial cells with a p55-selective mutant of human TNF-alpha (R32W-S86T) induced significant and concentration-dependent increases in endothelin-1 release. A \*\*\*p75\*\*\* receptor-selective TNF-alpha mutant (D143N-A145R) was ineffective alone or in combination with the p55-selective mutant. Competitive binding experiments with (125I)TNF-alpha showed the p55-selective mutant, but not the p75-selective mutant, to inhibit the binding of (125I)TNF-alpha to endothelial and HEp-2 cells. Similar results were obtained with the p55 agonist \*\*\*antibody\*\*\* \*\*\*htrl\*\*\* in both cell lines. These results establish the p55 TNF receptor as the main receptor involved in the induction of endothelin-1 synthesis by \*\*\*TNF\*\*\* -alpha.

2/7/2 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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14434776 BIOSIS NO.: 199800229023  
Activators of polymorphonuclear neutrophils modulate expression of the tumor necrosis factor-alpha p75 receptor  
AUTHOR: Zeman Krysztof (Reprint); Paleolog Ewa Maria; Tchorzewski Henryk  
AUTHOR ADDRESS: Dep. Clinical Immunology, Military Med. Acad., Pl. Hallera 1, 90-647 Lodz 39, Poland\*\*Poland  
JOURNAL: Central-European Journal of Immunology 22 (4): p272-277 1997 1997  
MEDIUM: print  
ISSN: 1426-3912  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Tumor necrosis factor-alpha is cytokine that mediates a variety of immune and inflammatory reactions and is reported to stimulate some functions of polymorphonuclear neutrophils (such as adherence, phagocytosis, degranulation, antibody-dependent cellular cytotoxicity, microbial killing and oxidative metabolism following binding to its specific cell surface receptors. Recent studies provide evidence for the existence of two distinct TNF receptor molecules, that contribute to a varying, extent to TNF binding by different human cells. In this report we have studied the expression of p55 and p75 TNF receptors on human PMN, using specific monoclonal \*\*\*antibodies\*\*\* of the Utr and \*\*\*Htr\*\*\* series. We found that resting human PMN after isolation procedures expressed mainly the 75 kDa \*\*\*TNF\*\*\* receptor. Activation of PMN by \*\*\*TNF\*\*\* -alpha, granulocyte-macrophage colony-stimulating factor and F-methionyl-leucyl-phenylalanine but not by phorbol ester, interferon-gamma (IFN-gamma) or calcium ionophore A23187 leads to a marked decrease in \*\*\*p75\*\*\* protein expression.

2/7/3 (Item 3 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13838712 BIOSIS NO.: 199799472772  
IL-4 and TNF-alpha-mediated proliferation of the human megakaryocytic line M-07e is regulated by induced autocrine production of GM-CSF  
AUTHOR: Wadhwa Meenu (Reprint); Dilger Paula; Meager Anthony; Walker Barry; Gaines-Das Rose; Thorpe Robin  
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JOURNAL: Cytokine 8 (12): p900-909 1996 1996  
ISSN: 1043-4666  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: In this study, the authors examined the effects of recombinant human interleukin 4 (rhIL-4) and recombinant human tumour necrosis factor alpha (rhTNF-alpha) alone or in combination on proliferation of the human cytokine dependent myeloid cell line, M-07e. While rhIL-4 or rhTNF-alpha alone induced only a weak proliferative response, a synergistic proliferative signal was clearly evident on stimulation of cells with a combination of both cytokines. The stimulatory effect of rhTNF-alpha is mediated predominantly by the 55-kDa TNF receptor because the agonistic monoclonal \*\*\*antibody\*\*\* \*\*\*htr\*\*\* -9 and the Trp-32 Thr. TNF-alpha mutant protein specific for this receptor type produced similar results to rhTNF-alpha. In contrast, the Asn-143 Arg-145 TNF-alpha mutant protein specific for the 75-kDa TNF receptor produced only minimal proliferation of M-07e cells. Using RT-PCR, we found that rhTNF-alpha rapidly and strongly induced granulocyte-macrophage colony-stimulating factor (GM-CSF) mRNA production, while rhIL-4 was a slow and less efficient inducer of GM-CSF mRNA. However, there was little evidence of the TNF-alpha/IL-4 combination acting synergistically on GM-CSF mRNA production as the levels of GM-CSF mRNA increased only marginally compared with IL-4 or TNF-alpha alone. Thus, the observed synergistic effect of TNF-alpha/IL-4 costimulation of M-07e cells seems to be mediated via induction of GM-CSF secretion rather than an enhanced production of GM-CSF mRNA. Higher levels of GM-CSF were detectable in supernatants of cells treated with both rhIL-4 and rhTNF-alpha than in cells stimulated with either cytokine alone. Furthermore, addition of a neutralising antibody against GM-CSF abrogated the observed synergistic effect of rhIL-4 and rhTNF-alpha treatment, indicating that the rhIL-4/TNF-alpha combination acts to significantly increase GM-CSF release which then acts in an autocrine manner to enhance the proliferation of M-07e cells.

2/7/4 (Item 4 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13685482 BIOSIS NO.: 199799319542  
The role of receptors for tumour necrosis factor-alpha in the induction of human polymorphonuclear neutrophil chemiluminescence  
AUTHOR: Zeman Krzysztof (Reprint); Kantorski Jerzy; Paleolog Ewa M; Feldmann Marc; Tchorzewski Henryk  
AUTHOR ADDRESS: Dep. Clin. Immunol., Military Acad., Pl. Hallera I, 90-647 Lodz 9, Poland\*\*Poland  
JOURNAL: Immunology Letters 53 (1): p45-50 1996 1996  
ISSN: 0165-2478  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Tumour necrosis factor-alpha (TNF-alpha) is a potent mediator of inflammation, which exerts profound effects on polymorphonuclear neutrophils (PMN). TNF-alpha binds to distinct cell surface receptors termed p55 and p75, expressed in approximately equal amounts on the PMN surface. We have studied the effects of TNF-alpha on the priming of F-Met-Leu-Phe (FMLP)-stimulated oxidative metabolism of PMN, using a luminol-enhanced chemiluminescence assay, and have examined the relative

roles of PMN receptors for TNF-alpha in priming this oxidative metabolism, using antibodies with p55 and p75 receptor-specific agonistic and antagonistic activities. We have obtained' the following results: (1) Antibody Htr-9 with agonistic activity at the p55 receptor mimicked the effect of TNF-alpha; however, a combination of Htr-9 and TNF-alpha did not result in any further increase in chemiluminescence relative to the response observed with TNF-alpha alone. The \*\*\*p75\*\*\* agonistic antibody MR2-1 actually decreased basal and FMLP-enhanced chemiluminescence. Additionally, MR2-1 substantially inhibited the effects of both TNF-alpha itself and of the p55 agonist \*\*\*Htr\*\*\* -9. (2) Addition of antibodies with antagonistic activities at the p55 (antibody TBP-2) and p75 (antibody Utr-1) receptors resulted in a marked inhibition of the PMN response to \*\*\*TNF\*\*\* -alpha. A combination of both Utr-1 and TBP-2 was most effective at inhibiting the action of \*\*\*TNF\*\*\* . We have confirmed previously published observations that TNF-alpha alone effectively stimulates the oxidative metabolism of PMN in vitro, and that pre-incubation of PMN with TNF-alpha enhances subsequent generation of oxidative metabolites in response to FMLP. We conclude that both p55 and p75 receptors play a critical role in mediating the activation of PMN by TNF-alpha.

2/7/5 (Item 5 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13598086 BIOSIS NO.: 199699232146  
Evidence for exclusive role of the p55 tumor necrosis factor (TNF) receptor in mediating the TNF-induced collagenase expression by human dermal fibroblasts  
AUTHOR: Rekdal Oystein (Reprint); Osterud Bjarne; Svendsen John Sigurd; Winberg Jan-Olof  
AUTHOR ADDRESS: Dep. Biotechnol., Inst. Med. Biol., Univ. Tromso, N-9037 Tromso, Norway\*\*Norway  
JOURNAL: Journal of Investigative Dermatology 107 (4): p565-568 1996 1996  
ISSN: 0022-202X  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: The aim of this study was to examine the roles of the TNF receptors p55 and p75 in the TNF-enhanced expression of collagenase by human dermal fibroblasts. The agonistic p55 monoclonal antibody Htr9 and TNF induced production of similar amounts of collagenase. Polyclonal or monoclonal agonistic \*\*\*p75\*\*\* antibodies failed to enhance collagenase production, and the antagonistic p75 antibody 5E12 did not inhibit TNF-enhanced expression of collagenase. This strongly suggests that p55, but not p75, is involved in TNF-induced production of collagenase. Cells continued to produce an elevated level of collagenase after the removal of \*\*\*TNF\*\*\* or \*\*\*Htr9\*\*\* . These data suggest that it may be useful to use specific inhibitors of collagenase rather than to block cytokine action directly in the treatment of diseases with chronic enhanced collagenolytic activity. A peptide of residues 36-62 of TNF previously reported to be chemotactic to leukocytes was also able to enhance the expression of collagenase activity by dermal fibroblasts. Thus, design of peptides with specific TNF effects may offer a novel approach for treatment of fibrotic disorders.

2/7/6 (Item 6 from file: 5)  
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13509258 BIOSIS NO.: 199699143318  
Activation of the TNF-alpha-p55 receptor induces myocyte proliferation and modulates agonist-evoked calcium transients in cultured human tracheal smooth muscle cells  
AUTHOR: Amrani Yassine (Reprint); Panettieri Reynold A Jr; Frossard Nelly; Bronner Christian  
AUTHOR ADDRESS: Univ. Pa. Med. Cent., Pulmonary and Critical Care Div., Dep. Med., East Gate Build., 3600 Spruce St., Philadelphia, PA 19104-4283, USA\*\*USA  
JOURNAL: American Journal of Respiratory Cell and Molecular Biology 15 (1): p55-63 1996 1996  
ISSN: 1044-1549  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Evidence suggests that cytokines may modulate smooth muscle cell function in a variety of inflammatory diseases. In the present study, we characterized the specific receptor subtypes that mediate tumor necrosis factor alpha (TNF-alpha) effects on myocyte proliferation and on agonist-induced calcium transients in cultured human tracheal smooth muscle cells (TSMC). Pretreatment of human TSMC with \*\*\*TNF\*\*\* -alpha potentiated cytosolic calcium ((Ca-2+)-i) transients evoked by carbachol. In a similar manner, selective TNF-alpha-p55 receptor agonists such as htr-9, an activating monoclonal antibody, or a recombinant TNF-p55 (rTNF-p55), which specifically activates the TNF -alpha-p55 receptor but not the TNF-alpha-p75 receptor, also augmented (Ca-2+)-i transients evoked by carbachol. In parallel experiments, TNF-alpha, rTNF-alpha-p55, and htr-9 induced human TSMC proliferation as measured by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. Interestingly, activation of the \*\*\*TNF\*\*\* -alpha- \*\*\*p75\*\*\* receptor with a selective agonist, recombinant TNF-alpha-p75 (rTNF-alpha-p75), or inhibition of the TNF-alpha-p75 receptor with utr-1, an inhibitory anti-TNF-alpha-p75 receptor antibody, had no effect on TNF-alpha-augmented calcium transients or on myocyte growth. To further confirm the receptor specificity of these findings, immunocytochemical studies were performed using receptor-specific \*\*\*antibodies\*\*\*. These studies demonstrated marked cell-surface expression of the TNF-alpha-p55 receptor compared with expression of the TNF-alpha-p75 receptor on human TSMC. Taken together, our results suggest that TNF-alpha modulates agonist-induced calcium transients and induces human TSMC proliferation by specific activation of the TNF-alpha-p55 receptor. Further studies addressing the cellular and molecular mechanisms regulating cytokine modulation of airway smooth muscle function may provide new insight into mechanisms that induce airway hyperresponsiveness in asthma.

2/7/7 (Item 7 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13326226 BIOSIS NO.: 199698794059  
A non-competitive P55 TNF receptor antibody enhances the specific activity of lymphotoxin-alpha  
AUTHOR: Medvedev A E; Laegreid A; Sundan A; Espevik T (Reprint)

AUTHOR ADDRESS: Inst. Cancer Res. Mol. Biol., Univ. Trondheim, N-7005  
Trondheim, Norway\*\*Norway  
JOURNAL: Scandinavian Journal of Immunology 43 (4): p439-448 1996 1996  
ISSN: 0300-9475  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: In the present study the authors elucidated the involvement of the two TNF receptors (TNFR) in discriminating TNF and lymphotoxin-alpha (LT-alpha) effects in human SW480-beta-Gal and KYM-1 cell lines. A non-competitive p55 TNFR monoclonal antibody (MoAb) 44E strongly enhanced LT-alpha-mediated gene regulation and cytotoxicity up to the level of the responses caused by \*\*\*TNF\*\*\*. \*\*\*TNF\*\*\*-induced biological responses were only weakly influenced by 44E. 44E did not affect both binding and the rate of dissociation of the cytokines. The combination of the two p55 TNFR MoAb 44E and Htr5 elicited strong TNF responses, while none of them were agonistic alone. When the \*\*\*p75\*\*\* TNFR was blocked with Utr1, LT-alpha was still less potent than \*\*\*TNF\*\*\* in mediating CMV promoter activation and cytotoxicity. However, the addition of 44E in the presence of Utr1 merged the LT-alpha dose-response curves with those obtained with TNF plus Utr1. Using antagonistic TNFR MoAb, the authors further showed that TNF functions through both TNFR types while LT-alpha mediates its effects largely via the p55 TNFR. These data suggest that LT-alpha is less potent than TNF due to its lower ability to properly trigger the p55 TNFR and because of its lack of signalling through the p75 TNFR.

2/7/8 (Item 8 from file: 5)  
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13031498 BIOSIS NO.: 199598499331  
Activation of neutrophil and eosinophil respiratory burst by tumor necrosis factor-alpha on biological surfaces  
AUTHOR: Patriarca Pierlivi (Reprint); Menegazzi R; Cramer R; Dri P; Busetto S; Decleva E  
AUTHOR ADDRESS: Ist. Patologia Generale, Univ. Trieste, Via A. Fleming 22, 34127 Trieste, Italy\*\*Italy  
JOURNAL: Regional Immunology 6 (5-6): p371-377 1994 (1995) 1994  
ISSN: 0896-0623  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Neutrophils (NEU) and eosinophils (EOS) are known to be stimulated in suspension by several agonists both particulate (for example, bacteria) or soluble (e.g., the phorbol esters) but not by cytokines, such as tumor necrosis factor-alpha (TNF) or colony stimulating factors. However, when adherent to selected biological surfaces, both NEU and EOS show a sizable response to TNF. In our setup surfaces precoated with fibronectin, fibrinogen, or fibrin, but not surfaces coated with laminin or endothelial cells, enable NEU or EOS to respond to TNF with superoxide anion (O<sub>2</sub><sup>-</sup>) release. The response is strictly adherence-dependent since it is inhibited by anti-beta-2 integrin mAbs (anti-CD18 mAbs). In addition, cell spreading appears to be a prerequisite for the metabolic response to occur. \*\*\*TNF\*\*\* activities are mediated by two distinct membrane receptors, the 55-kD receptor (p55) and the \*\*\*75\*\*\*-kD receptor (\*\*\*p75\*\*\*). NEU express both receptors but their role in the elicitation of the respiratory burst is not known.

Using mAbs that specifically inhibit TNF binding to p55 (mAbs htr-9 and H398) and to p75 (mAb utr-1) we have investigated the relative role of these receptors in TNF-induced O-2- production by NEU residing on fibronectin-coated surfaces. None of the \*\*\*antibodies\*\*\* affected \*\*\*TNF\*\*\* -induced O-2- production. MAb htr-9 and H398 alone stimulated production of substantial amounts of O-2- while mAb utr-1 did not. Anti-p55 mAbs were ineffective on NEU in suspension. NEU bound more mAb utr-1 than mAb \*\*\*htr\*\*\* -9, indicating that unresponsiveness to mAb utr-1 was not due to low or absent p75 expression. The agonistic effect of mAbs \*\*\*htr\*\*\* -9 and H398, in terms of time course, dependence on beta-2 integrin-mediated adherence, microfilament integrity, and sensitivity to elevations of intracellular levels of cAMP, was similar to the agonistic effect of \*\*\*TNF\*\*\* . These results suggest that TNF-induced triggering of respiratory burst by NEU residing on biological surfaces is under control of the p55 TNF receptor.

2/7/9 (Item 9 from file: 5)  
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12719254 BIOSIS NO.: 199598187087  
Modulation of monocyte antigen-presenting capacity by tumour necrosis factor-alpha (TNF): Opposing effects of exogenous TNF before and after an antigen pulse and role of TNF gene activation in monocytes  
AUTHOR: Kowalczyk Danuta; Mytar Bozena; Jasinski Marek; Pryjma Juliusz; Zembala Marek (Reprint)  
AUTHOR ADDRESS: Dep. Clin. Immunol., Inst. Peadiatr., Jagiellonian Univ. Med. Coll., Wielicka 265, 30-663 Cracow, Poland\*\*Poland  
JOURNAL: Immunology Letters 44 (1): p51-57 1995 1995  
ISSN: 0165-2478  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: We have previously shown that exogenous human recombinant tumour necrosis factor-alpha (rTNF), added before an antigen pulse, enhanced antigen presentation by human blood monocytes. The present study shows that, surprisingly, rTNF added after an antigen (PPD) pulse inhibited, while anti-TNF monoclonal antibody (mAb) enhanced, antigen presentation. mAbs \*\*\*htr\*\*\* -9 against p55 \*\*\*TNF\*\*\* receptor type I (TNF-RI) abrogated rTNF enhancing effect on PPD presentation and decreased presenting activity of untreated monocytes while htr-1 mAb, against p75 TNF receptor type II (TNF-RII), reversed the inhibitory effect of rTNF given after antigen pulse. PPD and rTNF when added singly induced \*\*\*TNF\*\*\* -mRNA accumulation in monocytes. Pretreatment of monocytes with rTNF followed by a PPD pulse caused an enhancement of \*\*\*TNF\*\*\* -mRNA accumulation. However, when post-treatment with rTNF was applied to PPD-pulsed monocytes, then inhibition of TNF gene expression was seen. This may point to the role of endogenously generated TNF in regulation of antigenpresenting capacity of monocytes. These studies indicate that TNF is an important regulator of monocyte antigen-presenting capacity and that the level of TNF gene activation in monocytes may be associated with their ability to present nominal antigen.

2/7/10 (Item 10 from file: 5)  
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12565810 BIOSIS NO.: 199598033643

Involvement of the tumor necrosis factor receptor p75 in mediating cytotoxicity and gene regulating activities

AUTHOR: Medvedev Andrei E; Sundan Anders; Espevik Terje (Reprint)

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JOURNAL: European Journal of Immunology 24 (11): p2842-2849 1994 1994

ISSN: 0014-2980

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Using agonistic antibodies (Ab) we have examined whether the 75-kDa chain of the tumor necrosis factor receptor (p75 TNFR) is capable of mediating cytotoxic response and gene regulation alone or in cooperation with p55 TNFR. Addition of an anti-p75 TNFR polyclonal antiserum or anti-p75 monoclonal antibody (mAb) plus anti-immunoglobulin (Ig) led to cytotoxic response of human KYM-1 rhabdomyosarcoma cells. Anti-p75 mAb alone had no effect pointing out the importance of strong receptor stimulation for signal transduction into the cell. Simultaneous triggering of both the p55 and \*\*\*p75\*\*\* TNFR by agonistic Ab resulted in additive cytotoxic action on KYM-1 cells. The anti-p75 mAb 3H5, directed to a non-TNF binding site on the human p75 TNFR, was used to confirm further the ability of the p75 TNFR to potentiate p55 TNFR-mediated cell death. While exhibiting no cytotoxicity by its own, 3H5 significantly augmented the cytotoxic effect of the anti-p55 mAb htr9 towards KYM-1 cells. Neither the anti- \*\*\*p75\*\*\* \*\*\*TNFR\*\*\* antiserum nor anti-p75 mAb were cytotoxic for human U937 cells suggesting that the cytolysis resulting from p75 TNFR cross-linking is cell specific. Noteworthy, stimulation of the \*\*\*p75\*\*\* \*\*\*TNFR\*\*\* with mAb plus anti-Ig or polyclonal antiserum led to a marked enhancement of the p55 TNFR-induced U937 cell death, indicating collaboration between the two TNFR in induction of cytotoxicity also in this cell line. However, 3H5 mAb did not affect the ability of anti-p55 mAb to lyse U937 cells. Altogether, these data demonstrate the difference between KYM-1 and U937 cell lines with respect to the role for the p75 TNFR in mediating cytotoxicity. Both TNFR were found to mediate cytomegalovirus (CMV) promoter activation in human SW480T-beta-Gal cells and nuclear transcription factor  $\kappa$ B (NF- $\kappa$ B) induction in this cell line as well as in KYM-1 cells. It was demonstrated for the first time that independent stimulation of both TNFR resulted in an additive effect on the CMV promoter activation and induction of the NF- $\kappa$ B. Taken together, these results indicate that the p75 TNFR induces cytotoxicity in a cell-specific manner and potentiates p55 TNFR-mediated cytotoxic response and gene regulation.

2/7/11 (Item 11 from file: 5)

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12533039 BIOSIS NO.: 199598000872

Functional activities of receptors for tumor necrosis factor-alpha on human vascular endothelial cells

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JOURNAL: Blood 84 (8): p2578-2590 1994 1994

ISSN: 0006-4971  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Tumor necrosis factor-alpha (TNF-alpha) plays a critical role in the control of endothelial cell function and hence in regulating traffic of circulating cells into tissues in vivo. Stimulation of endothelial cells in vitro by TNF-alpha increases the surface expression of leukocyte adhesion molecules, enhances cytokine production, and induces tissue factor procoagulant activity. In the present study, we have examined the relative roles of the two cell surface receptors for TNF-alpha (p55 and p75) on endothelial cells, using antibodies with both agonistic and antagonistic activities. We report that anti-p55 receptor agonistic antibody Htr-9 induces the expression of tissue factor antigen and the release of interleukin-8 (IL-8) and granulocyte-macrophage colony-stimulating factor (GM-CSF). In contrast, there is very little or no activation of endothelial cell responses by an anti- \*\*\*p75\*\*\* agonist. \*\*\*TNF\*\*\* -alpha-induced expression of tissue factor and adhesion molecules, and release of IL-8 and GM-CSF, are decreased by antibodies with antagonistic activities for either receptor, although the effect of anti-p55 antibodies is markedly greater than that of anti-p75 \*\*\*antibodies\*\*\*. The responses of endothelial cells to lymphotoxin/TNF-beta are significantly decreased by anti-p55 antagonists alone. Our data suggest that endothelial cell responses to TNF-alpha, such as expression of tissue factor and adhesion molecules for mononuclear cells, which may be important in the pathogenesis of atherosclerosis, are mediated predominantly, but not exclusively, by the p55 TNF receptor.

2/7/12 (Item 12 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12423301 BIOSIS NO.: 199497444586  
Lymphotoxin acts as an autocrine growth factor for Epstein-Barr virus-transformed B cells and differentiated Burkitt lymphoma cell lines  
AUTHOR: Gibbons Deena L; Rowe Martin; Cope Andrew P; Feldmann Marc; Brennan Fionula M (Reprint)  
AUTHOR ADDRESS: Kennedy Inst. of Rheumatol., Sunley Building, 1 Lurgan Ave., Hammersmith, London W6 8LW, UK\*\*UK  
JOURNAL: European Journal of Immunology 24 (8): p1879-1885 1994 1994  
ISSN: 0014-2980  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: A critical event in B cell immortalization by Epstein-Barr virus (EBV) is the establishment of an autocrine loop where cells produce a growth factor which supports their own proliferation. We investigated the potential of lymphoblastoid cell lines (LCL) and Burkitt lymphoma (BL) cell lines to produce and respond to the cytotoxins, tumor necrosis factor-alpha (TNF-alpha) and lymphotoxin (LT). Transformation in vitro of peripheral blood B cells by EBV from seven different donors resulted in spontaneous production of both LT (11542 pg/ml +/- 7546, mean +/- SD) and, to a lesser extent, TNF-alpha (197 pg/ml +/- 174). Similarly BL cell lines derived from in vivo transformation which developed a 'LCL-like' phenotype in vitro (group M) produced more LT (1990 pg/ml +/- 1740) than the group I' BL cell lines (lt 40 pg/ml LT) which had maintained the original BL biopsy cell phenotype in vitro. Transformation of peripheral

blood B cells to generate LCL also resulted in an increase in surface p75 (p lt 0.02) and to a lesser extent p55 (not significant, ns) TNF receptor (TNF-R) expression. Similar increases in surface TNF-R (p75 p lt 0.02, p55 ns) were observed on the 'group In' BL cell lines compared with the 'group I' BL cell lines. Proliferation of an LCL and a 'group HI' BL cell line in vitro was via an autocrine loop since inhibition of LT reduced proliferation. This proliferation could also be blocked in the presence of the antagonistic anti-p55 TNF-R antibody, H398, but not the antagonistic antibody anti-p75 TNF-R antibody UTR-1. Furthermore, proliferation could be induced with the p55 agonistic \*\*\*antibody\*\*\* , \*\*\*HTR\*\*\* -9. In contrast to these observations with p55 TNF-R antibodies, two out of six of the 'group III' BL lines (Jijoye and Oba) only expressed the p75 TNF-R and proliferation of these cells could only be blocked by the antagonistic anti- \*\*\*p75\*\*\* \*\*\*TNF\*\*\* -R \*\*\*antibody\*\*\* UTR-1. These data suggest which display an LCL phenotype. Furthermore, although both TNF-R are increased on the surface of these cells, this autocrine growth signal is mediated principally through binding to the p55 TNF-R.

2/7/13 (Item 13 from file: 5)  
 DIALOG(R)File 5:Biosis Previews(R)  
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12377747 BIOSIS NO.: 199497399032  
 Evidence that tumor necrosis factor alpha (TNF)-induced activation of neutrophil respiratory burst on biologic surfaces is mediated by the p55 TNF receptor  
 AUTHOR: Menegazzi Renzo; Cramer Rita; Patriarca Pierluigi; Scheurich Peter; Dri Pietro (Reprint)  
 AUTHOR ADDRESS: Istituto di Patologia Generale, via A. Fleming 22, 34127 Trieste, Italy\*\*Italy  
 JOURNAL: Blood 84 (1): p287-293 1994 1994  
 ISSN: 0006-4971  
 DOCUMENT TYPE: Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English

ABSTRACT: Polymorphonuclear leukocytes (PMN) residing on biologic surfaces respond with a vigorous respiratory burst when exposed to tumor necrosis factor alpha ( \*\*\*TNF\*\*\* ). PMN possess both the p55 and the p75 \*\*\*TNF\*\*\* receptors, but their role in the elicitation of the respiratory burst is not known. We addressed this problem by studying the effect of monoclonal antibodies (MoAbs) directed against the p55 TNF receptor (MoAb H398 and MoAb htr-9) and the p75 TNF receptor (MoAb utr-1) on TNF-induced production of O-2- by PMN residing on fibronectin-coated surfaces. Neither the anti-p55 nor the anti- \*\*\*p75\*\*\* MoAbs affected TNF-induced O-2- production despite their known ability to competitively inhibit TNF binding to the corresponding receptor. Experiments with the antibodies alone showed that the anti-p55 MoAbs directly triggered PMN O-2- production, whereas no response was elicited by the anti- \*\*\*p75\*\*\* MoAb. PMN unresponsiveness to the anti-p75 MoAb could not be ascribed to low expression of p75 receptor, because binding of the anti-p75 MoAb utr-1 to PMN was, indeed, even higher than binding of the anti-p55 MoAb \*\*\*htr\*\*\* -9. The agonistic activity of the anti-p55 MoAbs was comparable with that of TNF and was not or only minimally modified by the simultaneous presence of \*\*\*TNF\*\*\* . Triggering of the respiratory burst by TNF was completely prevented by Fab fragments of the anti-p55 MoAb H398. Moreover, the monovalent Fab fragments, which lacked any stimulatory

effect on PMN O-2- production, acquired strong agonistic activity on cross-linking with anti Fab antibodies, suggesting that the ability of the anti-p55 antibodies to stimulate PMN O-2- production depends on their ability to cross-link the TNF receptors. The agonistic effect of the anti-p55 MoAbs was only observed with cells residing on fibronectin-coated surfaces and not with cells in suspension, and in terms of kinetics, dependence on beta-2 integrin-mediated adherence, microfilament integrity, and sensitivity to elevations of intracellular levels of cAMP, it was virtually indistinguishable from the agonistic effect of TNF. Taken together, these results suggest that the p55 receptor is responsible for TNF-induced triggering of the respiratory burst of PMN residing on biologic surfaces.

2/7/14 (Item 14 from file: 5)  
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12336554 BIOSIS NO.: 199497357839  
Role of the 75 kD- and 55 kD-receptors in tumour necrosis factor mediated cytotoxicity and its regulation by dexamethasone and by 1,25-dihydroxyvitamin D-3 in U937 cells  
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JOURNAL: European Cytokine Network 4 (4): p285-292 1993 1993  
ISSN: 1148-5493  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: The respective role of p55 and of p75 TNF receptors in mediating the constitutive or the regulated cytotoxic response of U937 cells was discriminated using monoclonal antibodies directed against each receptor type, respectively \*\*\*htr\*\*\* -9 and utr-1. Cytotoxicity was mediated by the p55 receptors. The \*\*\*p75\*\*\* receptors were also implicated as it reduced 100 fold the maximal active dose of rTNF-alpha and 15 fold the EC-50 value. Dexamethasone potentiated and 1,25-dihydroxyvitamin D-3 abolished rTNF-alpha induced cell growth arrest and toxicity. Dexamethasone was required to be present for rTNF-alpha to be active. It increased the maximal response whether toxicity was mediated through only p55 or both p55 and p75 receptors, without changing the respective EC-50 values for rTNF-alpha. Therefore dexamethasone did not affect the interactions between p55 and p75 receptors nor between these receptors and their ligand, suggesting that it regulates the cytotoxicity at a post-receptor level. 1,25-dihydroxyvitamin D-3 drove the promonocytic U937 cells resistant to rTNF-alpha by short-term effect. Comparing the effect of 1,25-dihydroxyvitamin D-3 and 1,25-dihydroxyvitamin D-3 derivatives on the cytotoxicity to their effect on cell surface receptor expression, revealed that the capacity to induce resistance to rTNF-alpha was restricted to those steroids which downregulated the p55 receptors. Therefore, resistance to rTNF-alpha could be related to an early effect of 1,25-dihydroxyvitamin D-3 on p55 receptors. Finally, the results suggest that dexamethasone and 1,25-dihydroxyvitamin D-3 regulate TNF-alpha induced cytotoxicity by affecting processes probably related to the functions of the p55 receptors.

2/7/15 (Item 15 from file: 5)

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12207596 BIOSIS NO.: 199497228881

Ceramide does not mediate the effect of tumour necrosis factor alpha on superoxide generation in human neutrophils

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JOURNAL: Biochemical Journal 298 (3): p733-738 1994 1994

ISSN: 0264-6021

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The effect of turnout necrosis factor alpha (TNF-alpha) on superoxide generation in human neutrophils was investigated using the Nitro Blue Tetrazolium reduction assay. TNF-alpha stimulated superoxide generation in a time- and concentration-dependent fashion. The maximally effective concentration of TNF-alpha for superoxide generation was 10 nM and maximal response was obtained after 15-20 min. The monoclonal antibody (mAb), utr-1, which was raised against the 75 kDa receptor and behaves as an antagonist, had no effect on superoxide generation, but partially inhibited the response to \*\*\*TNF\*\*\* -alpha. mAb htr-9, which was raised against the 55 kDa receptor and behaves as an agonist, mimicked the effect of TNF-alpha, but with a lower maximal response. As it has been reported that ceramide might act as a second messenger to mediate many of the effects of TNF-alpha, the effects of exogenous sphingomyelinase and the cell-permeable ceramide analogue, C-2-ceramide, on production of superoxide anions, induction of priming in response to formylmethionyl-leucyl-phenylalanine, and cell-shape change were examined. Neither sphingomyelinase nor C-2-ceramide mimicked the effect of TNF-alpha. Ceramide is converted into ceramide 1-phosphate by ceramide kinase and we have measured levels of this metabolite to clarify the effect of TNF-alpha on sphingomyelinase activity in neutrophils. Although exogenous sphingomyelinase increased the amount of ceramide 1-phosphate in a time-dependent manner, and C-2-ceramide was rapidly converted into C-2-ceramide phosphate, TNF-alpha had no effect on the level of ceramide 1-phosphate. These results suggest that TNF-alpha stimulates superoxide generation through both the 55 kDa and 75 kDa receptors, but that ceramide does not act as an intracellular mediator for TNF-alpha in human neutrophils.

2/7/16 (Item 16 from file: 5)

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12173160 BIOSIS NO.: 199497194445

Regulation of monocyte chemoattractant protein-1 expression in adult human non-neoplastic astrocytes is sensitive to tumor necrosis factor (TNF) or antibody to the 55-kDa TNF receptor

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JOURNAL: Journal of Neuroimmunology 50 (1): p101-107 1994 1994

ISSN: 0165-5728

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RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Infiltration of the central nervous system (CNS) by monocytes is a characteristic of many non-malignant disease processes, although the signals regulating such traffic are unclear. Tumor necrosis factor (TNF) and other inflammatory cytokines have been shown to elicit production of monocyte chemoattractant activity in glioma cells, but the regulation of such activity in non-neoplastic adult astrocytes has not been examined. We previously observed that TNF constituted a proliferative signal for non-neoplastic adult human astrocytes in vitro involving the 55-kDa TNF receptor. In the present study, we demonstrate that \*\*\*TNF\*\*\* exposure enhances the expression of monocyte chemoattractant protein-1 (MCP-1) mRNA and functional monocyte chemoattractant activity in non-neoplastic astrocytes. Results indicated that MCP-1 mRNA expression was maximal within 3 h, and was further augmented by the protein synthesis inhibitor cycloheximide (CY). \*\*\*Antibody\*\*\* ( \*\*\*htr\*\*\* -9) directed against the 55-kDa TNF receptor also elicited MCP-1 mRNA expression while antibody to the 75-kDa TNF receptor (utr-1) was ineffective. Secretion of monocyte chemoattractant activity was significantly greater in TNF- or htr-9-treated astrocytes than in utr-1-treated or untreated controls; activity was abolished by treatment with \*\*\*antibody\*\*\* to MCP-1. These findings suggest that non-neoplastic adult human astrocytes may contribute to CNS inflammatory responses by mediating recruitment of peripheral blood monocytes.

2/7/17 (Item 17 from file: 5)  
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12152426 BIOSIS NO.: 199497173711  
Lymphotoxin lacks effects on 75-kDa receptors in cytotoxicity on U-937 cells  
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JOURNAL: Biochemical and Biophysical Research Communications 199 (1): p 70-77 1994 1994  
ISSN: 0006-291X  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: We examined differences in cytotoxic activity between human lymphotoxin (LT) and tumor necrosis factor (TNF) as functions of their interaction with two types of TNF receptors, 55-kDa (p55R) and 75-kDa (p75R). Cytotoxic activity of LT was much lower than that of TNF on a human monocytic cell line, U-937, on which p75R was predominant. Monoclonal antibodies specific for p55R ( \*\*\*htr\*\*\* -5 and htr-9) and p75R (utr-1) significantly diminished TNF cytotoxicity, whereas, utr-1 was only slightly inhibitory to LT cytotoxicity, and \*\*\*htr\*\*\* -5 reduced it significantly. \*\*\*TNF\*\*\* individual binding to p75R increased cytotoxic activity when p55R was occupied by htr-9 and a mutein of TNF which significantly lost affinity to \*\*\*p75R\*\*\*. However, LT binding to \*\*\*p75R\*\*\* did not increase. Scatchard analysis with (125I)LT and (125I) \*\*\*TNF\*\*\* showed that LT still had approximately half of the affinity to p75R and slightly less affinity to p55R than \*\*\*TNF\*\*\*. These results indicate slight cytotoxicity of LT compared to TNF, due to inability of LT to signal through p75R on U-937 cells without significant loss of affinity to \*\*\*p75R\*\*\*.

2/7/18 (Item 18 from file: 5)  
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11937204 BIOSIS NO.: 199396101620  
Roles of two tumor necrosis factor receptors in induction of  
differentiation of ML-1 cells  
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JOURNAL: Anticancer Research 13 (4): p883-886 1993  
ISSN: 0250-7005  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: The individual roles of two types of TNF receptors (55 kDa  
and 75 kDa) in induction of differentiation of human myeloblastic  
leukemia ML-1 cells, were investigated using three monoclonal  
\*\*\*antibodies\*\*\*. The \*\*\*antibody\*\*\* \*\*\*htr\*\*\* -9, which recognizes  
the 55  
kDa receptor, induced differentiation of ML-1 cells. Utr-1, which  
recognizes the 75 kDa receptor, blocked 125I-TNF binding by  
about 80% and inhibited by about 80% the TNF-induced NBT reducing  
activity. \*\*\*Htr\*\*\* -5 recognizes the 55 kDa receptor, blocked 125I-  
TNF binding by about 20% and inhibited by about 60% the TNF  
-induced NBT reducing activity. The data suggest that either of the two  
TNF receptors alone can mediate signals for the differentiation of  
ML-1 cells, and that simultaneous stimulation of both receptors will  
induce differentiation more effectively.

2/7/19 (Item 19 from file: 5)  
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11842315 BIOSIS NO.: 199396006731  
Divergent responses of human astrocytoma and non-neoplastic astrocytes to  
tumor necrosis factor alpha involve the 55 KDa tumor necrosis factor  
receptor  
AUTHOR: Barna Barbara P (Reprint); Barnett Gene H; Jacobs Barbara S; Estes  
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JOURNAL: Journal of Neuroimmunology 43 (1-2): p185-190 1993  
ISSN: 0165-5728  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: The effects of tumor necrosis factor (TNF) on DNA synthesis,  
proliferation, and induction of gene/protein expression of TNF were  
compared in neoplastic and non-neoplastic adult human astrocytes.  
Previously, we demonstrated that TNF induced proliferative responses in  
non-neoplastic adult human astrocytes. In astrocytoma cells, however, TNF  
elicited both proliferative and cytostatic responses depending upon cell  
density and TNF concentration. This bimodal effect persisted even in a  
homogeneous, cloned astrocytoma cell line (STT-9C), and was inhibitable  
by neutralizing \*\*\*antibody\*\*\* to \*\*\*TNF\*\*\*. \*\*\*TNF\*\*\* treatment  
enhanced

expression of TNF mRNA in astrocytoma cells but not in non-neoplastic astrocytes, and cell-associated or secreted TNF was not detectable in any culture. The involvement of receptors in astrocyte responses to TNF was examined in serological studies using monoclonal antibodies Utr-1 to the 75 kDa, and Htr-9 to the 55 kDa \*\*\*TNF\*\*\* receptor. \*\*\*Antibody\*\*\* to the 55 kDa \*\*\*TNF\*\*\* receptor alone was able to mimic the effects of TNF in both neoplastic astrocyte cultures while antibody to the 75 kDa \*\*\*TNF\*\*\* receptor had no effect. These data indicate that the bimodal actions of TNF on human astrocytoma cells as well as the stimulatory effects on non-neoplastic adult astrocytes are regulated at least in part by the 55 kDa TNF receptor. Astrocyte TNF receptors, however, do not appear to constitute part of an autocrine growth pathway in either non-neoplastic or neoplastic human astrocytes.

2/7/20 (Item 20 from file: 5)  
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11785043 BIOSIS NO.: 199395087309

Expression and functional role of tumor necrosis factor receptors on leukemic cells from patients with type B chronic lymphoproliferative disorders

AUTHOR: Trentin Livio; Zambello Renato; Agostini Carlo; Siviero Fosca; Adami Fausto; Marcolongo Renzo; Raimondi Roberto; Chisesi Teodoro; Pizzolo Giovanni; Semenzato Gianpietro (Reprint)

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JOURNAL: Blood 81 (3): p752-758 1993

ISSN: 0006-4971

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Two receptors for tumor necrosis factor (TNF) with different molecular weight (75-Kd and 55-Kd) and binding affinity have been recently discovered. To investigate the distribution and the functional role of these receptors on leukemic B cells from hairy cell leukemia (HCL) and B-cell chronic lymphocytic leukemia (B-CLL) patients, we evaluated: (1) the cytofluorimetric pattern of uncultured and cultured leukemic B cells incubated with utr-1 and htr-9 monoclonal antibodies (MoAbs), which specifically recognize the 75-Kd and 55-Kd TNF receptors (TNFR), respectively; (2) the effect of TNF-alpha and TNF-beta on leukemic B cells in an in vitro proliferation assay; (3) the role of anti-TNFR MoAbs on TNF-alpha and TNF-beta-driven B-cell growth; and (4) the proliferative effect of utr-1 and htr-9 MoAbs on in vitro cultured leukemic cells. Our study shows that the high affinity ( \*\*\*75\*\*\* -Kd) but not the low affinity (55-Kd) TNFR molecules are expressed on freshly isolated leukemic B cells recovered from HCL and B-CLL patients. The expression of these receptors was neither upregulated nor downregulated by different stimuli, including TNF-alpha, TNF-beta, B-cell growth factor, and interleukin-2. TNF-alpha efficiently triggers the proliferation of HC and, to a lesser extent, the growth of B-CLL cells. TNF-beta was also able to transduce the proliferative signal in HCL, but not in B-CLL patients. TNF-alpha- and TNF-beta-driven B-cell proliferation was inhibited by the preincubation of leukemic B cells with utr-1 but not htr-9 MoAb. Moreover, anti-75-Kd, but not anti-55-Kd TNFR MoAb, was able to trigger the proliferation of leukemic B cells, and in particular of HC. These results show that leukemic B cells from patients

with HCL and B-CLL are equipped with a fully functional high affinity TNFR.

2/7/21 (Item 21 from file: 5)  
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11758447 BIOSIS NO.: 199395060713  
Tumor necrosis factor alpha stimulates sphingomyelinase through the 55 kDa receptor in HL-60 cells  
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AUTHOR ADDRESS: Dep. Pharmacol., Univ. Oxford, Mansfield Road, Oxford, OX1 3QT, UK\*\*UK  
JOURNAL: FEBS (Federation of European Biochemical Societies) Letters 314 (3): p297-300 1992  
ISSN: 0014-5793  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Tumor necrosis factor alpha (TNF-alpha) stimulated rapid (seconds) hydrolysis of sphingomyelin in HL-60 cells, formation of phosphocholine (PCho) and a decrease in choline. The response to TNF-alpha was concentration dependent with a maximal effect at 3-10 nM. The monoclonal \*\*\*antibody\*\*\* (mAb), \*\*\*htr\*\*\* -9, which behaves as an agonist at the 55 kDa subtype of the TNF receptor, also stimulated sphingomyelin hydrolysis in intact cells. In contrast, the mAb, utr-1, which behaves as an antagonist at the 75 kDa receptor subtype, had no effect on sphingomyelin hydrolysis either on its own or in the presence of \*\*\*TNF\*\*\* -alpha. In addition, \*\*\*htr\*\*\* -9 or \*\*\*TNF\*\*\* -alpha stimulated hydrolysis of sphingomyelin in a membrane fraction of HL-60 cells. These results are consistent with a role of sphingomyelin hydrolysis as an early event in the signalling mechanism of TNF -alpha, and suggest that this pathway is activated through the 55 kDa subtype of the \*\*\*TNF\*\*\* receptor.

2/7/22 (Item 22 from file: 5)  
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11736801 BIOSIS NO.: 199395039067  
Autocrine growth limitation of human papillomavirus type 16-harboring keratinocytes by constitutively released tumor necrosis factor-alpha  
AUTHOR: Malejczyk Jacek (Reprint); Malejczyk Magdalena; Koeck Andreas; Urbanski Agatha; Majewski Slawomir; Hunzelmann Nicolas; Jablonska Stefania; Orth Gerard; Luger Thomas A  
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JOURNAL: Journal of Immunology 149 (8): p2702-2708 1992  
ISSN: 0022-1767  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: TNF-alpha is known to exert antitumor and antiviral effects and to participate in the regulation of the immune response. In our study we demonstrate that human rTNF-alpha specifically blocks growth of SK-v keratinocyte cell line harboring and expressing human papillomavirus type

16 (HPV 16) sequences. This inhibitory effect was shown by (3H)TdR incorporation and cell counting. Binding experiments with 125I- \*\*\*TNF\*\*\*-alpha showed that SK-v cells express about 10,000 single class TNF-alpha-R per cell with affinity constant of about 0.7 nM. Binding of 125I-TNF-alpha could be inhibited by htr-9 mAb recognizing a 55/60-kDa type I TNF-alpha-R but not by utr-1 mAb recognizing 75/80-kDa type II TNF-alpha-R or irrelevant mAb specific for HPV16 E7 protein. Addition of anti- \*\*\*TNF\*\*\* - \*\*\*antibodies\*\*\* to SK-v cell culture resulted in significant (p lt 0.05), dose-dependent stimulation of their proliferation. SK-v cells constitutively expressed TNF-alpha mRNA, and SK-v CM contained TNF-alpha, as demonstrated by Northern block analysis, a specific ELISA, Western blot analysis, and a bioassay with TNF-alpha-sensitive L-M cells. HPLC gel filtration of SK-v cell CM showed that the factor cytotoxic for L-M cells coeluted with immunoreactive TNF-alpha. These results demonstrate that HPV16-harboring SK-v cells constitutively express and release immunoreactive and biologically active TNF-alpha that in turn may exert an autocrine growth inhibitory effect. This phenomenon could represent one of the self-limiting mechanisms controlling growth of HPV-induced neoplasia.

2/7/23 (Item 23 from file: 5)  
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11721717 BIOSIS NO.: 199395023983  
 Role of tumor necrosis factor-alpha and its specific 55-Kd and 75-Kd receptors in patients with lymphoproliferative disease of granular lymphocytes  
 AUTHOR: Zambello Renato; Trentin Livio; Bulian Pietro; Cassatella Marco; Raimondi Roberto; Chisesi Teodoro; Agostini Carlo; Semenzato Gianpietro (Reprint)  
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 JOURNAL: Blood 80 (8): p2030-2037 1992  
 ISSN: 0006-4971  
 DOCUMENT TYPE: Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English

ABSTRACT: The role of tumor necrosis factor-alpha (TNF-alpha) in the development of in vitro proliferative and cytotoxic abilities of granular lymphocytes (GL) in patients with lymphoproliferative disease of GL (LDGL) has been investigated. To this aim, taking advantage of the recent generation of specific monoclonal antibodies (MoAbs) reacting with the p55 and p75 TNF receptors (TNF-R) (htr-9 and utr-1 MoAb, respectively), we evaluated the expression and the functional role of each TNF-R in freshly isolated highly purified GL from a series of 10 LDGL patients (six CD3+ T-lineage GL and four CD3- natural killer (NK)-lineage GL). The expression of \*\*\*TNF\*\*\* -alpha transcripts and the release of TNF-alpha in the culture medium at resting conditions and following cell activation were also studied. Our data indicate that at resting conditions both CD3+ and CD3- GL express only the p75 \*\*\*TNF\*\*\* -R. Accordingly, a specific inhibition of phycoerythrin (PE)-conjugated TNF-alpha binding was demonstrated by the anti-p75 TNF-R utr-1 MoAb, but not by the anti-p55 htr-9 MoAb. Following activation with interleukin-2 (IL-2), anti-CD3, or anti-CD16 MoAbs, an increased expression of the p75 TNF-R and a slight induction of the p55 \*\*\*TNF\*\*\* -R was observed. Weak expression of specific TNF-alpha transcripts was detected at resting conditions and on unstimulated cells, whereas both IL-2 or anti-CD3 MoAb

induced TNF-alpha mRNA. Under these in vitro conditions, detectable amounts of this cytokine were demonstrated in the culture supernatant of GL. The cytotoxic and proliferating activities mediated by IL-2 or anti-CD3 MoAb were dampened by anti-TNF-alpha antibody, suggesting a role for endogenous TNF-alpha in these functions. Both utr-1 and htr-9 MoAbs showed a moderate inhibition of proliferative activity, whereas cytotoxicity was not reduced. Taken together, our results suggest that TNF-alpha plays a role in the mechanisms leading to CD3+ and CD3- GL in vitro activation in patients with LDGL.

2/7/24 (Item 24 from file: 5)  
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11703786 BIOSIS NO.: 199395006052  
Involvement of tumor necrosis factor (TNF) receptors p55 and p75 in TNF responses of acute myeloid leukemia blasts in vitro  
AUTHOR: Delwel Ruud (Reprint); Van Buitenen Carin; Lowenberg Bob; Touw Ivo  
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JOURNAL: Blood 80 (7): p1798-1803 1992  
ISSN: 0006-4971  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Tumor necrosis factor (TNF)-alpha TNF-beta have multiple effects on human acute myeloid leukemia (AML) cells in vitro, including (1) synergistic stimulation of proliferation with interleukin-3 (IL-3) and granulocyte-macrophage colony-stimulating factor (GM-CSF) and upregulation of interleukin-3 (IL-3) and GM-CSF receptors; (2) inhibition of granulocyte-CSF (G-CSF)-induced growth and rapid downmodulation of G-CSF receptors; and (3) induction of autocrine growth. Recently, two distinct TNF receptors (TNF-Rs), TNF-R(p55) and TNF-R(p75), have been identified. In this study, we show that both receptor types may be expressed by AML blasts. It has been investigated whether the different effects of TNF on AML blasts can be explained by differential activation of the distinct \*\*\*TNF\*\*\* -R structures. For this purpose, we used the monoclonal antibodies THR-1 and HTR-9, specifically recognizing TNF-R(p55), and UTR-1, specific for TNF-R(\*\*\*p75\*\*\*). \*\*\*TNF\*\*\* -(alpha and -BETA) mediated synergistic activation with IL-3/GM-CSF, upregulation of IL-3GM=CSF receptors, inhibition of G-CSF/induced growth, and rapid downmodulation of G-CSF receptors exclusively result from activation of \*\*\*TNF\*\*\* -R(p55). In certain cases in which TNF-alpha, rather than TNF-beta, induces AML growth through an autocrine mechanism, both TNF-R(p55) and (\*\*\*p75\*\*\*) are involved. These data indicate that the variety of TNF responses observed in AML can only be partially explained by differential activation of the NF-R(p55) and (p75) structures, and that TNF-R(p55) and AML blasts can transduce both positive (synergism with IL-3/GM-CSF) and negative regulatory signals (inhibition of G-CSF-induced proliferation) following TNF activation.

2/7/25 (Item 25 from file: 5)  
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11431518 BIOSIS NO.: 199294133359  
THE TYPE B RECEPTOR FOR TUMOR NECROSIS FACTOR-ALPHA MEDIATES DNA FRAGMENTATION IN HL-60 AND U937 CELLS AND DIFFERENTIATION IN HL-60 CELLS

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JOURNAL: Blood 80 (5): p1339-1346 1992  
ISSN: 0006-4971  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

ABSTRACT: Tumor necrosis factor- $\alpha$  (TNF) binds to two specific cell surface receptors, types A and B, which are both present on HL-60 and U937 cells, and induces monocytoid differentiation in HL-60 cells and early DNA fragmentation in HL-60 and U937 cells. To further define the receptors roles, we studied how monoclonal antibodies (MoAbs) against each receptor affected \*\*\*TNF\*\*\* -induced cellular responses. HTR-9, an MoAb against the type B (low affinity, 55 Kd) receptor, reproduced all of these effects in a dose-dependent manner. UTR-1, an MoAb against the type A (high affinity, 75 Kd) receptor, had no effect in saturating doses, but supersaturating doses enhanced DNA fragmentation threefold. \*\*\*TNF\*\*\* and interferon gamma (IFN- $\gamma$ ) synergistically induced morphologic differentiation and monocytic antigen expression, while the antitype B receptor MoAb was synergistic for morphologic response, but not antigen expression. Our results indicate that (1) the type B receptor mediates some responses to TNF in HL-60 and U937 cells, (2) the type A receptor does not stimulate these responses, (3) the TNF molecule is not necessary for some of these actions, and (4) TNF-induced morphologic changes and surface antigen expression in HL-60 cells may be regulated by separate postreceptor pathways.

2/7/26 (Item 26 from file: 5)  
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11372021 BIOSIS NO.: 199294073862  
ENHANCED EXPRESSION OF TUMOR NECROSIS FACTOR RECEPTOR MRNA AND PROTEIN IN MONONUCLEAR CELLS ISOLATED FROM RHEUMATOID ARTHRITIS SYNOVIAL JOINTS  
AUTHOR: BRENNAN F M (Reprint); GIBBONS D L; MITCHELL T; COPE A P; MAINI R N ; FELDMANN M  
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JOURNAL: European Journal of Immunology 22 (7): p1907-1912 1992  
ISSN: 0014-2980  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

ABSTRACT: We previously proposed the hypothesis that the pro-inflammatory cytokine tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) plays a pivotal role in the pathogenesis of rheumatoid arthritis (RA) based on our observations that is the dominant inducer of interleukin-1 (IL-1) and granulocyte-macrophage colony-stimulating factor (GM-CSF) production in RA synovial joint mononuclear (MNC) cells in culture. Since \*\*\*TNF\*\*\* - $\alpha$  acts via two membrane receptors, we have extended those studies to investigate the distribution of the p55 and p75 TNF receptors ( \*\*\*TNF\*\*\* -R) in RA tissue. Surface receptor expression was quantitated by flow cytometry using monoclonal antibodies specific to the p55 ( \*\*\*HTR\*\*\* -9) and the \*\*\*p75\*\*\* (UTR-1) \*\*\*TNF\*\*\* -R. Both receptors were significantly increased on MNC isolated from the synovial membrane of RA patients compared to normal or RA peripheral blood MNC. Interestingly, the p75 TNF-R was increased both on large

monocytic/macrophage-type cells and CD3+ lymphocytes. Furthermore, there was a significant increase in the proportion of CD3+ cells in RA synovial fluid expressing the p75 TNF-R, compared to matched peripheral blood MNC. In contrast to RA synovial MNC, p75 or p55 TNF-R expression was not significantly increased in osteoarthritis synovial MNC. In addition, Northern blot analysis indicated abundant expression of both p55 and p75 mRNA in RA synovial joint MNC. This was in contrast to normal peripheral blood MNC cells which contained little or no constitutive TNF-R mRNA; following stimulation with phytohemagglutinin and IL-2, a rapid and transient expression of both receptor mRNA was induced. These results, therefore, indicate that in RA synovial joint tissue there is up-regulation of both p55 and p75 TNF-R mRNA and surface protein expression, and with the presence of TNF- $\alpha$  in RA tissues, these results provide support to our hypothesis that TNF- $\alpha$  is of critical importance in the pathogenesis of RA.

2/7/27 (Item 27 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10759212 BIOSIS NO.: 199192004983  
INDEPENDENT REGULATION OF 55-KDA AND 75-KDA TUMOR NECROSIS FACTOR RECEPTORS  
DURING ACTIVATION OF HUMAN PERIPHERAL BLOOD B LYMPHOCYTES  
AUTHOR: ERIKSTEIN B K (Reprint); SMELAND E B; BLOMHOFF H K; FUNDERUD S;  
PRYDZ K; LESSLAUER W; ESPEVIK T  
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3, NORW\*\*NORWAY  
JOURNAL: European Journal of Immunology 21 (4): p1033-1038 1991  
ISSN: 0014-2980  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

ABSTRACT: We have studied the expression of two different tumor necrosis factor receptors (TNFR; 55 kDa and 75 kDa) on resting and activated human peripheral blood B lymphocytes using specific monoclonal antibodies (mAb). Flow cytometric analysis revealed that most resting B cells expressed small amounts of the 75-kDa TNFR, and that the 75-kDa TNFR was markedly up-regulated upon stimulation with anti- $\mu$  or Staphylococcus aureus. Cowan strain I (SAC). In contrast, the expression of the 55-kDa TNFR was low on resting as well as on activated cells. B cell activation was accompanied by an increased binding of biotinylated TNF- $\alpha$ , and this binding could be blocked by preincubation of utr-1 (anti-75-kDa TNFR), but not the htr (anti-55-kDa TNFR) antibodies. Notably, a number of cytokines tested (interleukin 1 to 8, interferon- $\gamma$ , \*\*\*TNF\*\*\* - $\alpha$  and  $\beta$ ) did not influence the expression of either the 75-kDa or the 55-kDa TNFR when given to resting B cells. Moreover, phorbol 12-myristate 13-acetate led to an early, marked down-regulation of the 75-kDa TNFR expression, followed by a later modest increase after >24 h. In contrast to other cell systems where htr mAb have been found either to mimic or to inhibit TNF action, htr mAb had insignificant effects in assays or restimulation or preactivated B cells. However, utr-1 markedly inhibited the \*\*\*TNF\*\*\* - $\beta$  but only partly inhibited the \*\*\*TNF\*\*\* - $\alpha$  induced proliferation. Taken together, our data suggest that changes in 75-kDa protein expression is responsible for the increased \*\*\*TNFR\*\*\* expression on activated vs. resting peripheral blood B cells and that this protein also may play an important functional role.

2/7/28 (Item 28 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10644722 BIOSIS NO.: 199191027613  
PURIFICATION AND PARTIAL AMINO ACID SEQUENCE ANALYSIS OF TWO DISTINCT TUMOR  
NECROSIS FACTOR RECEPTORS FROM HL60 CELLS  
AUTHOR: LOETSCHER H (Reprint); SCHLAEGER E J; LAHM H-W; PAN Y-C E;  
LESSLAUER W; BROCKHAUS M  
AUTHOR ADDRESS: CENTRAL RES UNITS, F HOFFMANN-LA ROCHE LTD, ZFE/BIO 15/40,  
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JOURNAL: Journal of Biological Chemistry 265 (33): p20131-20138 1990  
ISSN: 0021-9258  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

ABSTRACT: Two distinct tumor necrosis factor (TNF) receptors of 55- and 75-kDa apparent molecular masses previously identified on the cell surface by monoclonal antibodies have been solubilized with Triton X-100 from HL60 cells. A filter-based dot blot assay was developed to monitor specific <sup>125</sup>I-TNF $\alpha$  binding during fractionation of the cell extract. By a combination of immuno- and ligand affinity chromatography and reverse phase high performance liquid chromatography both receptor proteins were purified to apparent homogeneity. Analysis by sodium dodecyl sulfate-polyacrylamide gel electrophoresis showed two bands at 55 and 51 kDa for the 55-kDa TNF receptor and a major 75-kDa and a minor 65-kDa band for the \*\*\*75\*\*\* -kDa \*\*\*TNF\*\*\* receptor. All these bands specifically bound \*\*\*TNF\*\*\*  $\alpha$  and \*\*\*TNF\*\*\*  $\beta$  in ligand blot experiments. The exclusive specificity of monoclonal \*\*\*antibodies\*\*\* of the utr series for the \*\*\*75\*\*\* -65-kDa bands and of the \*\*\*htr\*\*\* series for the 55-51-kDa bands was demonstrated with the purified antigens on Western blots. Both \*\*\*TNF\*\*\* receptor types were found to contain N-linked carbohydrates. N-terminal amino acid sequence analysis of the 55- and 51-kDa bands of the 55-kDa TNF receptor revealed identical sequences suggesting a possible truncation at the C-terminal end. Two different N-terminal sequences were determined for the 65-kDa band. One corresponded to the published sequence of ubiquitin; the other was therefore assumed to be a unique sequence of the 75-kDa TNF receptor. Additional internal sequences of this receptor were determined after proteolytic cleavage.

2/7/29 (Item 29 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10622184 BIOSIS NO.: 199191005075  
BINDING AND REGULATION OF CELLULAR FUNCTIONS BY MONOCLONAL ANTIBODIES  
AGAINST HUMAN TUMOR NECROSIS FACTOR RECEPTORS  
AUTHOR: SHALABY M R (Reprint); SUNDAN A; LOETSCHER H; BROCKHAUS M;  
LESSLAUER W; ESPEVIK T  
AUTHOR ADDRESS: GENENTECH INC, 460 POINT SAN BRUNO BLVD, SOUTH SAN  
FRANCISCO, CALIF 94080, USA\*\*USA  
JOURNAL: Journal of Experimental Medicine 172 (5): p1517-1520 1990  
ISSN: 0022-1007  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

ABSTRACT: The present study was undertaken to further characterize the

interaction of monoclonal antibodies (mAbs) against tumor necrosis factor (TNF) receptors with different targets, and to assess their ability to influence TNF effects on U937 and human endothelial cell (HEC) functions. Actions or recombination \*\*\*TNF\*\*\* - $\alpha$  on U937 and HEC were effectively inhibited by Htr-5 and Utr-1, and to a greater extent by a combination of both mAbs. The observations indicate that TNF interaction with antigenically different components of membrane receptors (p55 and p75) represents a crucial step in transduction of signals for TNF toxicity against U937 and TNF activation of HEC functions.

2/7/30 (Item 30 from file: 5)  
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10231409 BIOSIS NO.: 199090015888  
IDENTIFICATION OF TWO TYPES OF TUMOR NECROSIS FACTOR RECEPTORS ON HUMAN CELL LINES BY MONOCLONAL ANTIBODIES  
AUTHOR: BROCKHAUS M (Reprint); SCHOENFELD H-J; SCHLAEGER E-J; HUNZIKER W; LESSLAUER W; LOETSCHER H  
AUTHOR ADDRESS: CENTRAL RES UNITS, F HOFFMAN-LA ROCHE AG, 4002 BASEL, SWITZERLAND\*\*SWITZERLAND  
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 87 (8): p3127-3131 1990  
ISSN: 0027-8424  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

ABSTRACT: The pleiotropic cyto/lymphokine tumor necrosis factor (TNF) exerts its functions by binding to specific cell-surface receptors. We have prepared two sets of monoclonal antibodies (mAbs) against TNF-binding proteins from the HL-60 (htr-mAb series) and U-937 (utr-mAb series) cell lines. The \*\*\*htr\*\*\* antibodies inhibit the binding of <sup>125</sup>I-labeled \*\*\*TNF\*\*\* - $\alpha$  to HL-60 cells only partially, whereas they block the \*\*\*TNF\*\*\* - $\alpha$  binding to several adenocarcinoma cell lines (HEp-2, HeLa, and MCF7) almost completely. In contrast, the utr antibodies have no effect on \*\*\*TNF\*\*\* - $\alpha$  binding to the adenocarcinoma cell lines but partially inhibit \*\*\*TNF\*\*\* - $\alpha$  binding to HL-60 and U-937 cells. However, \*\*\*htr\*\*\* - $\beta$  and utr-1 antibodies in combination fully inhibit the \*\*\*TNF\*\*\* - $\alpha$  binding to HL-60 and U-937 cells. The binding of \*\*\*TNF\*\*\* - $\beta$  to HEp-2 and U-937 cells is also inhibited by \*\*\*htr\*\*\* and utr antibodies. Neither \*\*\*htr\*\*\* nor utr mAb has an effect on the TNF-sensitive murine cell lines L929 and WEHI 164. Flow cytometry studies show that mAbs \*\*\*htr\*\*\* - $\beta$  and utr-1 detect two distinct \*\*\*TNF\*\*\* -binding sites on human cell lines. Immunologic blot and immunoprecipitation analyses indicate that mAbs \*\*\*htr\*\*\* - $\beta$  and utr-1 recognize proteins of  $\approx$ 55 kDa and 75 kDa, respectively. These data provide evidence for the existence of two distinct TNF receptor molecules that contribute to varying extent to the \*\*\*TNF\*\*\* binding by different human cells.

2/7/31 (Item 1 from file: 73)  
DIALOG(R)File 73:EMBASE  
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0076771155 EMBASE No: 1997064113  
IL-4 and TNF- $\alpha$ -mediated proliferation of the human megakaryocytic line M-07e is regulated by induced autocrine production of GM-CSF

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Cytokine ( CYTOKINE ) (United Kingdom) December 1, 1996, 8/12 (900-909)  
CODEN: CYTIE ISSN: 1043-4666  
DOI: 10.1006/cyto.1996.0121  
DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract  
LANGUAGE: English SUMMARY LANGUAGE: English  
NUMBER OF REFERENCES: 52

In this study, the authors examined the effects of recombinant human interleukin 4 (rhIL-4) and recombinant human tumour necrosis factor alpha (rhTNF-alpha) alone or in combination on proliferation of the human cytokine dependent myeloid cell line, M-07e. While rhIL-4 or rhTNF-alpha alone induced only a weak proliferative response, a synergistic proliferative signal was clearly evident on stimulation of cells with a combination of both cytokines. The stimulatory effect of rhTNF-alpha is mediated predominantly by the 55-kDa TNF receptor because the agonistic monoclonal antibody htr-9 and the Trp SUB 32 Thr SUB 86 TNF-alpha mutant protein specific for this receptor type produced similar results to rhTNF-alpha. In contrast, the Asn SUB 143 Arg SUB 145 TNF-alpha mutant protein specific for the 75-kDa TNF receptor produced only minimal proliferation of M-07e cells. Using RT-PCR, we found that rhTNF-alpha rapidly and strongly induced granulocyte-macrophage colony-stimulating factor (GM-CSF) mRNA production, while rhIL-4 was a slow and less efficient inducer of GM-CSF mRNA. However, there was little evidence of the TNF-alpha/IL-4 combination acting synergistically on GM-CSF mRNA production as the levels of GM-CSF mRNA increased only marginally compared with IL-4 or TNF-alpha alone. Thus, the observed synergistic effect of TNF-alpha/IL-4 costimulation of M-07e cells seems to be mediated via induction of GM-CSF secretion rather than an enhanced production of GM-CSF mRNA. Higher levels of GM-CSF were detectable in supernatants of cells treated with both rhIL-4 and rhTNF-alpha than in cells stimulated with either cytokine alone. Furthermore, addition of a neutralising antibody against GM-CSF abrogated the observed synergistic effect of rhIL-4 and rhTNF-alpha treatment, indicating that the rhIL-4/TNF-alpha combination acts to significantly increase GM-CSF release which then acts in an autocrine manner to enhance the proliferation of M-07e cells.

2/7/32 (Item 2 from file: 73)  
DIALOG(R)File 73:EMBASE  
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0075520694 EMBASE No: 1993300250  
Role of the 75 kD- and 55 kD-receptors in tumour necrosis factor mediated cytotoxicity and its regulation by dexamethasone and by 1,25-dihydroxyvitamin D SUB 3 in U937 cells  
Chambaut-Guerin A.-M.; Guerrier M.; Thomopoulos P.  
INSERM U282, Hopital Henri Mondor, 94010 Creteil, France  
CORRESP. AUTHOR/AFFIL: Chambaut-Guerin A.-M.: INSERM U282, Hopital Henri Mondor, 94010 Creteil, France

European Cytokine Network ( EUR. CYTOKINE NETW. ) (France) October 26, 1993, 4/4 (285-292)  
CODEN: ECYNE ISSN: 1148-5493

DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract  
LANGUAGE: English SUMMARY LANGUAGE: English

The respective role of p55 and of p75 TNF receptors in mediating the constitutive or the regulated cytotoxic response of U937 cells was discriminated using monoclonal antibodies directed against each receptor type, respectively \*\*\*htr\*\*\* -9 and utr-1. Cytotoxicity was mediated by the p55 receptors. The \*\*\*p75\*\*\* receptors were also implicated as it reduced 100 fold the maximal active dose of rTNF-alpha and 15 fold the EC SUB 50 value. Dexamethasone potentiated and 1,25-dihydroxyvitamin D SUB 3 abolished rTNF-alpha induced cell growth arrest and toxicity. Dexamethasone was required to be present for rTNF-alpha to be active. It increased the maximal response whether toxicity was mediated through only p55 or both p55 and p75 receptors, without changing the respective EC SUB 50 values for rTNF-alpha. Therefore dexamethasone did not affect the interactions between p55 and p75 receptors nor between these receptors and their ligand, suggesting that it regulates the cytotoxicity at a post-receptor level. 1,25-dihydroxyvitamin D SUB 3 drove the promonocytic U937 cells resistant to rTNF-alpha by short-term effect. Comparing the effect of 1,25-dihydroxyvitamin D SUB 3 and 1,25-dihydroxyvitamin D SUB 3 derivatives on the cytotoxicity to their effect on cell surface receptor expression, revealed that the capacity to induce resistance to rTNF-alpha was restricted to those steroids which down-regulated the p55 receptors. Therefore, resistance to rTNF-alpha could be related to an early effect of 1,25 dihydroxyvitamin D SUB 3 on p55 receptors. Finally, the results suggest that dexamethasone and 1,25 dihydroxyvitamin D SUB 3 regulate TNF-alpha induced cytotoxicity by affecting processes probably related to the functions of the p55 receptors.

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PLEASE ENTER A COMMAND OR BE LOGGED OFF IN 5 MINUTES

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Set	Items	Description
S1	87	(HTR?)(10N)(ANTIBOD? OR HYBRIDOMA? OR IMMUNOGLOBULIN?)(20N- ) (75? OR P75?)(20N)(TNF?)
S2	32	RD S1 (unique items)

? e au=brockhaus.in.

Ref	Items	Index-term
E1	1	AU=BROCKHAUS W.L.
E2	4	AU=BROCKHAUS WOLFGANG
E3	0	*AU=BROCKHAUS.IN.
E4	2	AU=BROCKHAUS-DUMKE A
E5	10	AU=BROCKHAUS-DUMKE A.
E6	18	AU=BROCKHAUS-DUMKE ANKE
E7	1	AU=BROCKHAUS-PRUCHNIEWICZ U
E8	1	AU=BROCKHAUS-PRUCHNIEWICZ U.
E9	1	AU=BROCKHAUS-PRUCHNIEWICZ ULRIKE
E10	1	AU=BROCKHAUS-PRUCHNIEWICZ, ULRIKE
E11	1	AU=BROCKHAUS, A
E12	67	AU=BROCKHAUS, A.

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Ref	Items	Index-term
E1	3	AU=BROCKHAUS L
E2	164	AU=BROCKHAUS M
E3	0	*AU=BROCKHAUS M ?
E4	69	AU=BROCKHAUS M.
E5	29	AU=BROCKHAUS MANFRED

E6 1 AU=BROCKHAUS N.  
 E7 2 AU=BROCKHAUS NINA  
 E8 1 AU=BROCKHAUS P  
 E9 8 AU=BROCKHAUS R  
 E10 3 AU=BROCKHAUS R H  
 E11 4 AU=BROCKHAUS R.  
 E12 1 AU=BROCKHAUS RALPH

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? s e2-e5

164 AU=BROCKHAUS M  
 0 AU=BROCKHAUS M ?  
 69 AU=BROCKHAUS M.  
 29 AU=BROCKHAUS MANFRED

S3 262 E2-E5

? s s3 and (tnf?) and (htr? or utr?)(20n)(antibod? or immunoglobulin? or hybridoma?)

262 S3  
 272208 TNF?  
 10683 HTR?  
 38292 UTR?  
 2336912 ANTIBOD?  
 883389 IMMUNOGLOBULIN?  
 55195 HYBRIDOMA?  
 876 (HTR? OR UTR?)(20N)((ANTIBOD? OR IMMUNOGLOBULIN?) OR  
 HYBRIDOMA?)

S4 15 S3 AND (TNF?) AND (HTR? OR UTR?)(20N)(ANTIBOD? OR  
 IMMUNOGLOBULIN? OR HYBRIDOMA?)

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S5 5 RD S4 (unique items)

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5/7/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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11430532 BIOSIS NO.: 199294132373

FUNCTIONAL CHARACTERIZATION OF THE HUMAN TUMOR NECROSIS FACTOR RECEPTOR P75  
 IN A TRANSFECTED RAT-MOUSE T CELL HYBRIDOMA

AUTHOR: VANDENABEELE P (Reprint); DECLERCQ W; VERCAMMEN D; VAN DE CRAEN M;  
 GROOTEN J; LOETSCHER H; BROCKHAUS M; LESSLAUER W; FIERIS W

AUTHOR ADDRESS: RIJKSUNIVERSITEIT GENT, TEDEGANCKSTRAAT 35, B-9000 GENT,  
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JOURNAL: Journal of Experimental Medicine 176 (4): p1015-1024 1992

ISSN: 0022-1007

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: We investigated the biological role of the human tumor necrosis factor p75 (hTNF-R75), making use of the species specificity of TNF responses in murine (m) T cell lines. Several \*\*\*TNF\*\*\* -mediated activities on mouse T cells, such as cytokine induction or proliferation, showed a 100-500-fold difference in specific biological activity between mTNF and hTNF. After transfection of hTNF-R75 cDNA in a rat/mouse T cell hybridoma (PC60), however, the 100-fold lower specific biological activity of hTNF was converted to the same specific biological activity as mTNF. The \*\*\*TNF\*\*\* -mediated induction of granulocyte/macrophage colony-stimulating factor was strongly synergized by the addition of

interleukin 1. In the presence of the latter cytokine, ligand-competing monoclonal antibodies against hTNF-R75 (utr-1, utr-2, \*\*\*utr\*\*\* -3) were agonistic on transfected PC60 cells. This agonistic activity was further enhanced by crosslinking with sheep anti-murine \*\*\*immunoglobulin\*\*\* \*\*\*antibodies\*\*\*. These data provide direct evidence for a functional role of TNF-R75, without ligand-dependent TNF-R55 involvement, in the induction of cytokine secretion in T cells.

5/7/2 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10676123 BIOSIS NO.: 199191059014  
EXPRESSION OF THE TYPES A AND B TUMOR NECROSIS FACTOR TNF RECEPTORS IS INDEPENDENTLY REGULATED AND BOTH RECEPTORS MEDIATE ACTIVATION OF THE TRANSCRIPTION FACTOR NF-KAPPA-B TNF-ALPHA IS NOT NEEDED FOR INDUCTION OF A BIOLOGICAL EFFECT VIA TNF RECEPTORS  
AUTHOR: HOHMANN H-P (Reprint); BROCKHAUS M; BAEUERLE P A; REMY R; KOLBECK R; VAN LOON A P G M  
AUTHOR ADDRESS: CENTRAL RES UNIT, BUILD 15-6A, F HOFFMANN-LA ROCHE LTD, GRENZACHERSTRASSE 124, CH-4002 BASEL, SWITZERLAND\*\*SWITZERLAND  
JOURNAL: Journal of Biological Chemistry 265 (36): p22409-22417 1990  
ISSN: 0021-9258  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

ABSTRACT: The expression and biological function of the types A and B tumor necrosis factor (TNF) receptors were studied using three cell types. SW480T, HEP2, and HL60 cells had, respectively, mainly the type A, only the type B, and roughly similar amounts of both receptors. Dibutyric cAMP treatment induced a 3-6-fold increase in the amount of the type A receptor B receptor. Expression of both receptors can thus be regulated independently. HEP2 and human umbilical vein endothelial cells only showed the type B receptor, and expression of the type A receptor could not be induced in these cells. HL60 cells showed, upon Scatchard analysis, a single binding site for \*\*\*TNF\*\*\*  $\alpha$ , and its Kd may correspond to that of the type A receptor. The approximately 7-fold lower affinity of \*\*\*TNF\*\*\*  $\alpha$  binding to the type B receptor of HL60 cells was only detected after blocking all \*\*\*TNF\*\*\*  $\alpha$  binding to the type A receptor. Both the types A and B receptors mediated \*\*\*TNF\*\*\*  $\alpha$ -induced activation of the transcription factor NF-KB. The agonistic antibody htr9 to the type B receptor also activated NF-KB. Thus, signal transduction via the type B receptor may only require interaction with the receptor's extracellular domain.

5/7/3 (Item 3 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10644722 BIOSIS NO.: 199191027613  
PURIFICATION AND PARTIAL AMINO ACID SEQUENCE ANALYSIS OF TWO DISTINCT TUMOR NECROSIS FACTOR RECEPTORS FROM HL60 CELLS  
AUTHOR: LOETSCHER H (Reprint); SCHLAEGER E J; LAHM H-W; PAN Y-C E; LESSLAUER W; BROCKHAUS M  
AUTHOR ADDRESS: CENTRAL RES UNITS, F HOFFMANN-LA ROCHE LTD, ZFE/BIO 15/40, CH-4002 BASEL, SWITZERLAND\*\*SWITZERLAND  
JOURNAL: Journal of Biological Chemistry 265 (33): p20131-20138 1990

ISSN: 0021-9258  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

ABSTRACT: Two distinct tumor necrosis factor (TNF) receptors of 55- and 75-kDa apparent molecular masses previously identified on the cell surface by monoclonal antibodies have been solubilized with Triton X-100 from HL60 cells. A filter-based dot blot assay was developed to monitor specific  $^{125}\text{I}$ -TNF $\alpha$  binding during fractionation of the cell extract. By a combination of immuno- and ligand affinity chromatography and reverse phase high performance liquid chromatography both receptor proteins were purified to apparent homogeneity. Analysis by sodium dodecyl sulfate-polyacrylamide gel electrophoresis showed two bands at 55 and 51 kDa for the 55-kDa TNF receptor and a major 75-kDa and a minor 65-kDa band for the 75-kDa TNF receptor. All these bands specifically bound TNF $\alpha$  and TNF $\beta$  in ligand blot experiments. The exclusive specificity of monoclonal antibodies of the utr series for the 75·65-kDa bands and of the htr series for the 55·51-kDa bands was demonstrated with the purified antigens on Western blots. Both TNF receptor types were found to contain N-linked carbohydrates. N-terminal amino acid sequence analysis of the 55- and 51-kDa bands of the 55-kDa TNF receptor revealed identical sequences suggesting a possible truncation at the C-terminal end. Two different N-terminal sequences were determined for the 65-kDa band. One corresponded to the published sequence of ubiquitin; the other was therefore assumed to be a unique sequence of the 75-kDa TNF receptor. Additional internal sequences of this receptor were determined after proteolytic cleavage.

5/7/4 (Item 4 from file: 5)  
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10231409 BIOSIS NO.: 199090015888  
IDENTIFICATION OF TWO TYPES OF TUMOR NECROSIS FACTOR RECEPTORS ON HUMAN CELL LINES BY MONOCLONAL ANTIBODIES  
AUTHOR: BROCKHAUS M (Reprint); SCHOENFELD H-J; SCHLAEGER E-J; HUNZIKER W; LESSLAUER W; LOETSCHER H  
AUTHOR ADDRESS: CENTRAL RES UNITS, F HOFFMAN-LA ROCHE AG, 4002 BASEL, SWITZERLAND\*\*SWITZERLAND  
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 87 (8): p3127-3131 1990  
ISSN: 0027-8424  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

ABSTRACT: The pleiotropic cyto/lymphokine tumor necrosis factor (TNF) exerts its functions by binding to specific cell-surface receptors. We have prepared two sets of monoclonal antibodies (mAbs) against TNF-binding proteins from the HL-60 (htr-mAb series) and U-937 ( \*\*\*utr\*\*\* -mAb series) cell lines. The \*\*\*htr\*\*\* \*\*\*antibodies\*\*\* inhibit the binding of  $^{125}\text{I}$ -labeled \*\*\*TNF\*\*\* - $\alpha$  to HL-60 cells only partially, whereas they block the \*\*\*TNF\*\*\* - $\alpha$  binding to several adenocarcinoma cell lines (HEp-2, HeLa, and MCF7) almost completely. In contrast, the utr antibodies have no effect on TNF - $\alpha$  binding to the adenocarcinoma cell lines but partially inhibit \*\*\*TNF\*\*\* - $\alpha$  binding to HL-60 and U-937 cells. However, \*\*\*htr\*\*\* -9 and utr-1 antibodies in combination fully inhibit the

\*\*\*TNF\*\*\* - $\alpha$  binding to HL-60 and U-937 cells. The binding of  
\*\*\*TNF\*\*\* - $\beta$  to HEp-2 and U-937 cells is also inhibited by \*\*\*htr\*\*\*  
and \*\*\*utr\*\*\* antibodies\*\*\*. Neither \*\*\*htr\*\*\* nor \*\*\*utr\*\*\*  
mAb has

an effect on the \*\*\*TNF\*\*\* -sensitive murine cell lines L929 and WEHI 164.  
Flow cytometry studies show that mAbs htr-9 and utr-1 detect two distinct  
\*\*\*TNF\*\*\* -binding sites on human cell lines. Immunologic blot and  
immunoprecipitation analyses indicate that mAbs htr-9 and utr-1 recognize  
proteins of  $\approx$ 55 kDa and 75 kDa, respectively. These data provide  
evidence for the existence of two distinct TNF receptor molecules  
that contribute to varying extent to the TNF binding by different  
human cells.

5/7/5 (Item 5 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10165532 BIOSIS NO.: 199089083423  
CHARACTERIZATION OF BINDING AND BIOLOGICAL EFFECTS OF MONOCLONAL ANTIBODIES  
AGAINST A HUMAN TUMOR NECROSIS FACTOR RECEPTOR  
AUTHOR: ESPEVIK T (Reprint); BROCKHAUS M; LOETSCHER H; NONSTAD U;  
SHALABY R  
AUTHOR ADDRESS: INST CANCER RES, UNIV TRONDHEIM, REGIONSYKEHUSET, N-7006  
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JOURNAL: Journal of Experimental Medicine 171 (2): p415-426 1990  
ISSN: 0022-1007  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

ABSTRACT: Three different antibodies against a human TNF  
receptor (htr-1, htr-5, and htr-9) have been examined  
for their binding pattern of U937 cells and ability to mimic TNF  
- $\alpha$  activity in U937 cells, Fs4 fibroblasts, and human endothelial  
cells. Flow cytometric analysis revealed that htr-5 and htr-9 bound  
specifically to a TNF receptor on U937 cells that could be blocked  
by pretreatment with rTNF- $\alpha$ . Pretreatment of U937 cells with  
rTNF- $\beta$  blocked the binding of htr-9, but to a lesser extent htr-5  
binding. Pretreatment with htr-5 inhibited the binding of htr-9 to U937  
cells while pretreatment with htr-9 did not inhibit htr-5 binding. These  
results indicate that htr-5 and htr-9 recognize distinct but overlapping  
epitopes of a human TNF receptor on U937 cells and that htr-5 may  
be close to a \*\*\*TNF\*\*\* - $\alpha$ -specific domain of the binding site.  
Pretreatment with htr-5 or htr-9 only minimally reduced  
binding of BrTNF- $\alpha$  to U937 cell; however, these \*\*\*antibodies\*\*\*  
were much more effective in inhibiting BrTNF- $\alpha$  binding to HL-60  
cells. Furthermore, it was found that \*\*\*htr\*\*\* -1 and htr-9, but not  
htr-5, had \*\*\*TNF\*\*\* - $\alpha$  activity on U937 cells, Fs4 fibroblasts, and  
endothelial cells and that the \*\*\*TNF\*\*\* - $\alpha$  activity induced by  
htr-9 was completely inhibited by htr-5. However, the cytotoxic activity  
of \*\*\*TNF\*\*\* - $\alpha$  was only partially inhibited by htr-5 on U937 cells  
while htr-5 had no effect on \*\*\*TNF\*\*\* - $\alpha$  activity on Fs4 cells. The  
data suggest that a common epitope is involved in inducing TNF  
- $\alpha$  activity in three different cell systems.

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